

## PRIOR AUTHORIZATION POLICY

**POLICY:** Chenodal™ (chenodiol tablets – Retrophin)

**TAC APPROVAL DATE:** 07/17/2019

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### OVERVIEW

Chenodiol is a naturally occurring bile acid. Chenodal (chenodiol tablets) is indicated for patients with radiolucent stones in well-opacifying gallbladders, in whom selective surgery would be undertaken except for the presence of increased surgical risk due to systemic disease or age.<sup>1</sup> Chenodal suppresses hepatic synthesis of both cholesterol and cholic acid, gradually replacing cholic acid and its metabolite (deoxycholic acid) in an expanded bile acid pool. This process contributes to biliary cholesterol desaturation and gradual dissolution of radiolucent cholesterol gallstones in the presence of a gallbladder visualized by oral cholecystography. The likelihood of successful dissolution is far greater if the stones are floatable (high cholesterol content) or small. In patients with non-floatable stones, dissolution is less likely and added weight should be given to the risk that more emergent surgery might result from a delay due to unsuccessful treatment.

Chenodal was approved as an abbreviated new drug application (ANDA) to a chenodiol product (Chenix® [chenodiol tablets]) approved in 1983 with a new drug application (NDA). This previously available product was discontinued by the manufacturer in 1997 because more effective drugs and devices were utilized in the management of gallstones.<sup>2-3</sup> The Food and Drug Administration (FDA) asked Manchester Pharmaceuticals to return chenodiol to the US market primarily to treat a small number of individuals with a rare disorder called cerebrotendinous xanthomatosis (CTX).

### Gallstones

The most widely used treatment for symptomatic gallstones is cholecystectomy.<sup>4</sup> Two naturally occurring bile acids are used in the treatment of gallstones: ursodeoxycholic acid (UrsoForte®, Urso-250®, [ursodiol tablets, generics], Actigall® [ursodiol capsules, generics]) and chenodeoxycholic acid/chenodiol (Chenodal).<sup>5</sup> These agents reduce biliary cholesterol; however, their exact mechanisms differ. Both Chenodal and ursodiol promote the gradual dissolution of radiolucent gallstones over a period of 6 months to 2 years.<sup>4</sup>

### Cerebrotendinous Xanthomatosis (CTX)

The FDA asked Manchester Pharmaceuticals to return chenodiol to the US market primarily to treat a small number ( $\leq 50$ ) of patients in the US with the rare disorder, CTX. CTX is a lipid storage disorder with various clinical manifestations including juvenile cataracts, tendon xanthomas, premature atherosclerosis, and progressive neurologic disturbance (e.g., ataxia, seizures, psychiatric disorders, and peripheral neuropathy).<sup>7</sup> Other conditions associated with CTX include osteoarthritis, skeletal fractures, pulmonary insufficiency, renal and hepatic calculi, and childhood chronic diarrhea. CTX is the result of a mutated enzyme (cytochrome P450 27-sterol hydroxylase [CYP27]) which is normally responsible for the conversion of cholesterol to cholic acid and chenodeoxycholic acid. In CTX, reduced synthesis of cholic- and chenodeoxycholic acids seem to result in failed feedback inhibition of cholesterol production, in turn leading to hallmark laboratory findings of the disorder: increased serum cholestanol concentrations and elevated urinary bile alcohols.<sup>6</sup> Replacement therapy with chenodiol inhibits abnormal bile acid synthesis and is most effective in reducing elevated plasma cholestanol concentrations and eliminating bile alcohols.<sup>7</sup>

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## **POLICY STATEMENT**

Prior authorization is recommended for prescription benefit coverage of Chenodal. All approvals are provided for 3 years unless otherwise noted below.

**Automation:** None.

## **RECOMMENDED AUTHORIZATION CRITERIA**

Coverage of Chenodal is recommended in those who meet the following criteria:

### **Food and Drug Administration (FDA)-Approved Indications**

1. **Gallstones.** Approve if the patient has tried or is currently using an ursodiol product.

### **Other Uses with Supportive Evidence**

2. **Cerebrotendinous Xanthomatosis (CTX).** Approve if Chenodal is prescribed by or in consultation with a metabolic specialist who treats patients with CTX (or a specialist who focuses in the treatment of CTX).

## **CONDITIONS NOT RECOMMENDED FOR APPROVAL**

Chenodal has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Combination Therapy with Cholbam™** (cholic acid capsules). There are no efficacy data available to support use of combination therapy with Chenodal and Cholbam.
2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

## **REFERENCES**

1. Chenodal™ tablets [prescribing information]. San Diego, CA: Retrophin.™; June 2015.
2. [Data on file] Manchester Pharmaceuticals, Inc™; January 4, 2010.
3. [Data on file] Manchester Pharmaceuticals, Inc™; January 5, 2010.
4. Gaby AR. Nutritional approaches to prevention and treatment of gallstones. *Altern Med Rev.* 2009;14(3):258-267.
5. Abraham S, Rivero HG, Erlikh IV, Griffith LF, and Hondamudi VK. Surgical and nonsurgical management of gallstones. *Am Fam Physician.* 2014;89(10):795-802.
6. Lorincz MT, Rainier S, Thomas D and Fink JK. Cerebrotendinous xanthomatosis: possible higher prevalence than previously recognized. *Arch Neurol.* 2005;62:1459-1463
7. Moghadasian MH, Salen G, Frohlich JJ, et al. Cerebrotendinous Xanthomatosis. *Arch Neurol.* 2002;59:527-529.

**HISTORY**

<b>Type of Revision</b>	<b>Summary of Changes*</b>	<b>TAC Approval Date</b>
Annual revision	Combination use of Chenodal with Cholbam added to an indication not recommended for approval.	04/13/2016
Annual revision	--	04/12/2017
Annual revision	No criteria changes	07/11/2018
Annual revision	No criteria changes	07/17/2019

TAC – Therapeutic Assessment Committee; \* For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>.