SmartPA Criteria Proposal

Drug/Drug Class:	Bile Salt Agents PDL Edit
First Implementation Date:	June 23, 2011
Proposed Date:	September 15, 2022
Prepared For:	MO HealthNet
Prepared By:	MO HealthNet/Conduent
Criteria Status:	☐ Existing Criteria ☒ Revision of Existing Criteria ☐ New Criteria

Executive Summary

Purpose: The MO HealthNet Pharmacy Program will implement a state-specific preferred drug list.

Why Issue Selected: Cholelithiasis (gallstones) occurs when either cholesterol or bilirubin precipitates out of bile solution to form crystallized pieces of bile in the gallbladder. In the United States (U.S.) almost 80% of individuals with gallstones have cholesterol stones. Gallstone diseases affect 10-15% of the U.S. population, with close to 1 million new cases diagnosed each year. Participants with gallstone diseases may be asymptomatic or present with biliary colic or complications of gallstone disease. Gallstone blockages of the cystic duct result in pain and inflammation, which may lead to fever, jaundice, and infections. Treatment is usually unnecessary if gallstones are not causing symptoms. If treatment is warranted, cholecystectomy is the most widely used therapy. Alternatively, dissolution of the stones by chemicals, ursodiol or chenodiol, is used rather than surgery. These oral agents thin the bile and allow stones to dissolve. In addition, ursodiol decreases cholesterol in bile and bile stones by reducing the secretion of cholesterol from the liver and the fractional reabsorption of cholesterol by the intestines. Use of pharmacologic therapy is limited to small stones which are predominantly composed of cholesterol, allowing for rapid and complete dissolution. The most common adverse effects include headache, diarrhea, constipation, dizziness, nausea, and dyspepsia.

Cholestasis is the decrease in bile flow due to impaired secretion by hepatocytes or obstruction of bile flow through intrahepatic or extrahepatic bile ducts. Cholestasis is categorized as either hepatocellular or obstructive. Hepatocellular cholestasis occurs when there is an impairment in the formation of bile and can be caused by hepatitis, alpha1-antitrypsin deficiency, total parental nutrition (TPN) use, or genetic disorders such as progressive familial intrahepatic cholestasis (PFIC). In obstructive cholestasis there is an impedance to bile flow after it is formed, this can be caused by biliary atresia, congenital bile duct anomalies, cholelithiasis, cholangitis, Alagille syndrome, and nonsyndromic ductal paucity. Presentation may vary depending on disease, but symptoms may include scleral icterus, elevated bilirubin, dark urine, cutaneous jaundice, and severe pruritus. Treatment involves pharmacologic therapy, dietary modification, and surgical intervention depending on the severity and cause of cholestasis.

Total program savings for the PDL classes will be regularly reviewed.

Program-Specific Information:	Preferred Agents	Non-Preferred Agents
	• Ursodiol	• Actigall® • Bylvay® • Chenodal® • Cholbam® • Livmarli® • Ocaliva® • Reltone® • Urso® • Urso Forte®

Type of Criteria: ☐ **Increased risk of ADE** ☒ **Preferred Drug List**
☒ **Appropriate Indications** ☐ **Clinical Edit**

Data Sources: ☐ **Only Administrative Databases** ☒ **Databases + Prescriber-Supplied**

Setting & Population

- Drug class for review: Bile Salt Agents
- Age range: All appropriate MO HealthNet participants

Approval Criteria

- Documented compliance on current therapy regimen **OR**
- Failure to achieve desired therapeutic outcomes with trial of 1 or more preferred agents
  - Documented trial period of preferred agents **OR**
  - Documented ADE/ADR to preferred agents
- For Cholbam: documented diagnosis of sterol nucleus synthesis or side-change synthesis disorder OR peroxisomal disorders with history of compliance with adjunct therapy
- For Bylvay and Livmarli:
  - Participant has documented baseline liver tests (ALT, AST, TB, DB, INR) **AND**
  - Prescribed by or in consultation with a hepatologist, gastroenterologist, or other specialist in the treated disease state **AND**
  - Documentation of presence of moderate to severe pruritus as evidenced by:
    - Whitington scale indicating score of at least 2 submitted by prescriber **OR**
    - ItchRO(Obs) scale indicating score of at least 2 submitted by participant or caregiver **AND**
  - Participant history demonstrates therapeutic trial of ursodiol (defined as 60/90 days)
  - Initial approval of prior authorization is for 6 months. Renewal of prior authorization for up to 1 year may be given following documentation of clinical benefit as evidenced by decrease in pruritus symptoms
  - For Bylvay:
    - Documentation of genetic testing confirming pathogenic variant indicating presence and type of PFIC
  - For Livmarli:
    - Participant has documented diagnosis of Alagille syndrome confirmed by either:
      - Genetic testing confirming pathogenic variant of *JAG1* or *NOTCH2* OR
      - Presence of ≥ 3 of the following clinical features:
        - Cholestasis
        - Ophthalmologic abnormalities
        - Characteristic facial features
        - Cardiac defect
        - Skeletal abnormalities

Denial Criteria

- Lack of adequate trial on required preferred agents
- For Bylvay and Livmarli:
  - History of liver transplant or decompensated cirrhosis
  - Participant (female of childbearing age) is pregnant
  - For Bylvay:
    - Documented genetic testing indicating PFIC Type 2 with *ABCB11* variants encoding for nonfunction or absence of BSEP-3
    - Dose exceeds 6 mg per day
  - For Livmarli:
    - Dose exceeds 3 mL per day
- Therapy will be denied if all approval criteria are not met

Required Documentation

Laboratory Results:	X	Progress Notes:	
MedWatch Form:		Other:	

Disposition of Edit

Denial: Exception Code "0160" (Preferred Drug List Edit)
Rule Type: PDL

Default Approval Period

1 year

References

- Evidence-Based Medicine Analysis: "Bile Salts (Gallstone Solubilizing Agents)", UMKC-DIC; March 2022.
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- Livmarli (maralixibat) [package insert]. Foster City, CA; Mirum Pharmaceuticals, Inc.; September 2021.
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- Facts and Comparisons eAnswers (online); 2022 Clinical Drug Information, LLC.