Reference number(s)
4862-A

SPECIALTY GUIDELINE MANAGEMENT

BYLVAY (odevixibat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Treatment of cholestatic pruritus in patients 12 months of age and older with Alagille syndrome (ALGS)
B. Treatment of pruritus in patients 3 months of age and older with progressive familial intrahepatic cholestasis (PFIC)

Limitations of Use: Bylvay may not be effective in a subgroup of PFIC type 2 patients with specific ABCB11 variants resulting in non-functional or complete absence of the bile salt export pump protein.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Initial requests: Genetic testing results confirming a diagnosis of progressive familial intrahepatic cholestasis (PFIC) or Alagille syndrome (ALGS), if applicable.
B. Continuation requests: Chart notes or medical record documentation showing benefit from therapy (e.g., improvement in pruritis).

III. EXCLUSIONS

Coverage will not be provided for members who have PFIC type 2 with variants in the *ABCB11* gene resulting in non-functional or complete absence of the bile salt export pump (BSEP) protein.

IV. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a hepatologist or gastroenterologist.

V. CRITERIA FOR INITIAL APPROVAL

A. Pruritus in progressive familial intrahepatic cholestasis (PFIC)
Authorization of 6 months may be granted for treatment of pruritis in progressive familial intrahepatic cholestasis (PFIC) when all of the following criteria are met:

1. Member has a confirmed molecular diagnosis of PFIC (e.g., mutations in *ATP8B1*, *ABCB11*, *ABCB4*, *TJP2*, *MYO5B*).

2. Member has evidence of cholestasis (e.g., elevated serum bile acid level).
3. Member does not have any other concomitant liver disease (e.g., biliary atresia, liver cancer, alternate non-PFIC related etiology of cholestasis).
4. Member has not received a liver transplant.
5. Member is 3 months of age or older.

B. Cholestatic pruritis in Alagille syndrome (ALGS)

Authorization of 6 months may be granted for treatment of cholestatic pruritis in Alagille syndrome (ALGS) when all of the following criteria are met:

1. Member has a diagnosis of ALGS established by one of the following (see Appendix for major clinical features of ALGS):
   i. Genetic testing (e.g., mutations in *JAG1, NOTCH2*)
   ii. Family history of ALGS and one or more major clinical features of ALGS
   iii. Bile duct paucity and three or more major clinical features of ALGS
   iv. Four or more major clinical features of ALGS
2. Member has evidence of cholestasis (e.g., elevated serum bile acid level).
3. Member does not have a history or presence of other concomitant liver disease (e.g., biliary atresia, PFIC, liver cancer).
4. Member has not received a liver transplant.
5. Member is 12 months of age or older.

VI. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) requesting continuation of therapy when the member is experiencing benefit from therapy (e.g., improvement in pruritis).

VII. OTHER

Member cannot use the requested medication concomitantly with any other ileal bile acid transporter (IBAT) inhibitor (e.g., Livmarli).

VIII. APPENDIX

Major clinical features of ALGS

1. Hepatic abnormality (e.g., cholestasis)
2. Cardiac abnormality (e.g., stenosis of the peripheral pulmonary artery and its branches)
3. Skeletal abnormality (e.g., butterfly vertebrae)
4. Ophthalmologic abnormality (e.g., posterior embryotoxon)
5. Characteristic facial features (e.g., triangular-shaped face with a broad forehead and a pointed chin, bulbous tip of the nose, deeply set eyes, and hypertelorism)
6. Vascular abnormalities (e.g., intracranial bleeds, systemic vascular anomalies)
7. Renal structural or functional abnormality (e.g., abnormally small size, cysts)

IX. REFERENCES

1. Bylvay [package insert]. Cambridge, MA: Ipsen Biopharmaceuticals, Inc.; February 2024.
2. McKiernan P, Bernabeu JQ, Girard M, et al. Opinion paper on the diagnosis and treatment of progressive familial intrahepatic cholestasis. *JHEP Rep.* 2023;6(1):1000949. doi: 10.1016/j.jhepr.2023.100949

3. Spinner NB, Gilbert MA, Loomes KM, et al. Alagille syndrome. GeneReviews® [Internet]. Published May 19, 2000. Last updated January 4, 2024. Accessed August 14, 2024.
4. Menon J, Shanmugam N, Vij M, et al. Multidisciplinary management of Alagille syndrome. *J Multidiscip Healthc.* 2022;15:353-364.
5. National Organization for Rare Disorders (NORD). Alagille syndrome. Rare Disease Database. https://rarediseases.org. Published 2024. Last updated January 30, 2024. Accessed August 27, 2024.
6. The Childhood Liver Disease Research Network. Alagille syndrome. https://childrennetwork.org/For-Physicians/Alagille-Syndrome-Information-for-Physicians. Accessed August 27, 2024.
7. The Childhood Liver Disease Research Network. Progressive familial intrahepatic cholestasis. https://childrennetwork.org/Clinical-Studies/Progressive-Familial-Intrahepatic-Cholestasis. Accessed March 25, 2024.