Protocol for Ileal Bile Acid Transporters (IBAT) Inhibitors

Addendum Approved October 2024

Bylvay® (odevixibat)
Livmarli® (maralixibat)

Background: Bylvay *and* ***Livmarli*** *are ileal bile acid transporter (IBAT) inhibitors indicated for the treatment of pruritus in patients with progressive familial intrahepatic cholestasis (PFIC)and for the treatment of cholestatic pruritis in patients with Alagille Syndrome (ALGS). The purpose of this addendum is to consolidate both protocols to ensure easier access to guidelines.*

Criteria for approval:

1. Patient has a diagnosis of one of the following that has been confirmed by genetic testing:
   a. Progressive familial intrahepatic cholestasis (PFIC), **OR**
   b. Alagille syndrome (ALGS)

2. Patient is of the FDA-labeled or compendial approved age

3. Patient has significant pruritus, if able to report

4. Patient has cholestasis, as indicated by at least ONE of the following:
   a. Total serum bile acid >3x the upper limit of normal (ULN) for age
   b. Conjugated bilirubin >1 mg/dL
   c. Fat soluble vitamin deficiency of unknown etiology
   d. Gamma Glutamyl Transferase (GGT) >3 × ULN for age
   e. Intractable pruritus explainable only by liver disease

5. Patient has no history of liver transplant

6. Medication is prescribed by or in consultation with a hepatologist, gastroenterologist, or another specialist with experience in treatment of the appropriate disease state

7. Patient has tried and has had an inadequate response, intolerance, or contraindication to treatment with ursodeoxycholic acid or other agents used for symptomatic relief of pruritus (e.g., antihistamine, rifampicin, cholestyramine).

8. Patient has no contraindication to the requested drug

9. Medication will not be used with other IBAT inhibitors

10. Patient's weight will be monitored

11. Medication is prescribed in accordance with a Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with a medically-appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer-reviewed evidence

Exclusion (Limitation of Use):

Bylvay and Livmarli may not be effective in PFIC type 2 patients with ABCB11 variants resulting in non-functional or complete absence of bile salt export pump protein (BSEP-3)

Continuation of therapy:

1. Patient is responding positively to therapy as evidenced by improvement in one of the following:
   a. Improvement in pruritus, if able to report
   b. Reduction of serum bile acids from baseline

2. Patient is not taking concurrently with other IBAT inhibitors

3. Patient's weight will be monitored

4. Medication is prescribed in accordance with a Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with a medically-appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer-reviewed evidence

Initial Approval Duration: 3 months

Renewal Approval Duration: 6 months

Quantity Level Limit: Reference Formulary for drug specific quantity level limits

References:

1. Bylvay [prescribing information]. Albireo Pharma Inc. Boston, MA 02109. July 2021
2. Livmarli [prescribing information]. Mirum Pharmaceuticals Inc. Foster City, CA. September 2021
3. Clinical Pharmacology® Gold Standard Series [Internet database]. Tampa FL. Elsevier 2019. Updated periodically
4. Gunaydin M and Cil ATB. Progressive familial intrahepatic cholestasis: diagnosis, management, and treatment. Hepat Med. 2018;10:95-104
5. Düll, M.M., Kremer, A.E. Newer Approaches to the Management of Pruritus in Cholestatic Liver Disease. Curr Hepatology Rep 19, 86–95 (2020). https://doi.org/10.1007/s11901-020-00517-x
6. Davit-Spraul A et al. Progressive familial intrahepatic cholestasis. Orphanet Journal of Rare Diseases 2009, 4:1;10.1186/1750-1172-4-1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2647530/ Accessed online on April 29, 2022
7. Kamath BM, et al. Systematic review: The epidemiology, natural history, and burden of Alagille syndrome. J Pediatr Gastroenterol Nutr. 2018; 67:148-156.
8. Diaz-Frias J, Kondamudi NP. Alagille Syndrome. [Updated 2023 Aug 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK507827/