Iowa PDL New Drug Review

Proprietary Name: Attruby®
Common Name: acoramidis HCl tablet
PDL Category: Amyloidosis Treatments

Pharmacology/Usage: Acoramidis, the active ingredient of Attruby®, is a selective stabilizer of transthyretin (TTR). Acoramidis binds TTR at thyroxine binding sites and slows dissociation of the TTR tetramer into its constituent monomers, the rate-limiting step in amyloidogenesis.

Indication: For the treatment of the cardiomyopathy of wild-type or variant transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular death and cardiovascular-related hospitalization.

There is no pregnancy category for this medication; however, the risk summary indicates that available data with use in pregnant women are not sufficient to establish a drug associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. The safety and efficacy of use in the pediatric population have not been established.

Dosage Form: Film-coated Tablets: 356mg (equivalent to 400mg acoramidis HCl).

Recommended Dosage: Take 712mg PO BID (with or without food). Swallow tablets whole; do not cut, crush, or chew.

Drug Interactions: Acoramidis is metabolized by UGT enzyme-mediated glucuronidation. Concomitant use of UGT inducers can potentially decrease acoramidis exposure. While acoramidis is not metabolized by CYP3A, strong CYP3A inducers can also induce UGT enzymes. Avoid concomitant use of Attruby® with UGT inducers and strong CYP3A inducers.

Acoramidis inhibits CYP2C9 and may result in an increase in CYP2C9 substrate concentrations when these drugs are co-administered. Consider more frequent monitoring of patients for evidence of increased exposure when Attruby® is co-administered with sensitive CYP2C9 substrates.

Box Warning: There is no box warning with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Attruby®) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.* The most frequently reported adverse events included diarrhea (4%) and upper abdominal pain (4.1%).

Contraindications: There are no contraindications listed with this product.

Manufacturer: BridgeBio Pharma, Inc.

Analysis: The efficacy of Attruby® was demonstrated in a multicenter, international, randomized, double-blind, placebo-controlled trial that include adult patients with wild-type or variant (hereditary or *de novo*) ATTR-CM (N=611).

Patients were randomized to receive Attruby® (N=409) or placebo (N=202) BID for 30 months. Treatment assignment was stratified by type of ATTR-CM (variant [ATTRv-CM] or wild-type [ATTRwt-CM]), NT-proBNP level, and estimated glomerular filtration rate (eGFR). The mean age of included patients was 77 years, while 90.8% were

male, 87.9% were white, 19% had a history of permanent pacemaker, and 58% had a history of atrial fibrillation. No significant imbalance in baseline characteristics was observed between the two treatment groups.

Patients were permitted to start open-label tafamidis after 12 months in the study. A total of 107 patients received tafamidis: 61 patients (14.9%) in the Attruby® arm and 46 patients (22.8%) in the placebo arm. The median time to initiation of tafamidis for these 107 patients was 17 months.

The primary composite endpoint included all-cause mortality (ACM) and cumulative frequency of cardiovascular-related hospitalizations (CVH) over 30 months, analyzed hierarchically using the stratified Finkelstein-Schoenfeld (F-S) test. The F-S test demonstrated a statistically significant reduction (p=0.018) in ACM and cumulative frequency of CVH in the Attruby® arm as compared with the placebo arm. All-cause mortality was reported in 19% in the Attruby® arm and 26% in the placebo arm. The majority (79%) of the deaths were cardiovascular. CVH was reported in 27% in the Attruby® arm and 43% in the placebo arm. The mean number of CVH events was 0.3 vs 0.6 per year. The majority (59%) of CVH were heart failure hospitalizations reported in 13% in the Attruby® group and 26% in the placebo group.

The treatment effect of Attruby® on functional capacity and health status was assessed by the 6 minute walk distance (6MWD) and the Kansas City Cardiomyopathy Questionnaire-Overall Summary score (KCCQ-OS), respectively. At month 30, the least square mean difference in change from baseline in 6MWD was 40 meters (p<0.0001) and change from baseline in KCCQ-OS was 10 points (p<0.0001).

The changes from baseline in 6MWD and KCCQ-OS were analyzed using the mixed model for repeated measures (MMRM) with treatment group, visit, genotype (ATTRv-CM or ATTRwt-CM), NT-proBNP level (≤3000 vs >3000 pg/ml), eGFR level (≥45 vs <45ml/min/1.73m^2) and treatment group-by-visit interaction as factors, and baseline value as covariate.

A Cox regression analysis indicated a 35.5% decrease in the risk of the composite of ACM or first CV hospitalization (HR 0.645).

Place in Therapy: Attruby® is a transthyretin stabilizer indicated for the treatment of the cardiomyopathy of wild-type or variant transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular death and cardiovascular-related hospitalization. The efficacy of Attruby® was demonstrated in a randomized, double-blind, placebo-controlled study. The primary composite endpoint included all-cause mortality (ACM) and cumulative frequency of cardiovascular-related hospitalizations (CVH) over 30 months, analyzed hierarchically using the stratified F-S test. The F-S test demonstrated a statistically significant reduction (p=0.018) in ACM and cumulative frequency of CVH in the Attruby® arm as compared with placebo. Attruby® offers a new treatment option for patients with this disease. Other agents considered comparators of Attruby® include tafamidis and vutrisiran. Direct comparisons have not been found between tafamidis, acoramidis, or vutrisiran, but in patients with ATTR cardiac amyloidosis these treatments reduce the risk of hospitalization while tafamidis and vutrisiran reduce the risk of mortality.[2]

Summary

It is recommended that Attruby® should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for use.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred**

References

[1] Attruby® [package insert]. Palo Alto, CA: BridgeBio Pharmac, Inc; 2024.
[2] UpToDate online. Cardiac amyloidosis: Treatment and prognosis. Accessed June 2025.