09-J5000-11

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Reviewed: 02/12/25

Revised: 00/00/00

Subject: Acoramidis (Attruby™)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Approximately 10,000 to 15,000 patients are diagnosed with hereditary transthyretin mediated (hATTR) amyloidosis in the United States. hATTR is a rare, progressive, and fatal multi-system illness caused by misfolding deposits of transthyretin (TTR), a protein produced by the liver. Over time, these deposits cause significant neurologic problems, functional limitations, and disability. These presentations include a predominantly neurologic phenotype (formerly known as familial amyloid polyneuropathy [FAP]), and a predominantly cardiac phenotype (formerly known as familial cardiomyopathy), although the majority of cases express both neurologic and cardiac manifestations. hATTR profoundly impacts all aspects of quality of life. Given that the disease may affect multiple organ systems and may progress rapidly, a wide variety of manifestations may include (but are not limited to) weight loss, wasting, difficulty walking, and alternating constipation and uncontrollable diarrhea. Some patients also develop cardiac complications, which can increase the risk of early death. The age of onset of symptoms, the types of problems patients experience, and the rate of progression vary significantly. Treatment options include liver transplant, diflunisal, tafamidis (Vyndamax, Vyndaqel), patisiran (Onpattro™), and inotersen (Tegsedi™).

Acoramidis (Attruby), a selective TTR stabilizer, was approved by the U.S. Food and Drug Administration (FDA) in November 2024 for use in the treatment of the cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis in adults to reduce cardiovascular deaths and cardiovascular-related hospitalization.

The efficacy of acoramidis was demonstrated in a multicenter, international, randomized, double-blind, placebo-controlled study in 611 adult patients with wild-type or variant (hereditary or de novo) ATTR-CM (NCT03860935).

Participants were randomized (2:1) to receive acoramidis 712 mg (n=409) or placebo (n=202) twice daily 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 study participants was 77 years, 90.8% were male, 87.9% were White, 4.7% Black or African American, 2.1% Asian, 5.3% race other, 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.

Participants were permitted to initiate open-label tafamidis after 12 months in the study. A total of 107 participants received tafamidis: 61 (14.9%) in the ACORAMIDIS arm and 46 (22.8%) in the placebo arm. The median time to initiation of tafamidis for these 107 participants 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 acoramidis arm versus the placebo arm. All-cause mortality was reported in 19% and 26% of participants in the acoramidis and placebo groups, respectively. The majority (79%) of the deaths were cardiovascular. Cardiovascular-related hospitalization was reported in 27% and 43% of participants in the acoramidis and placebo groups, respectively. 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% and 26% of the participants in the acoramidis and placebo groups, respectively.

The treatment effect of acoramidis on functional capacity and health status was assessed by the 6MWD and the Kansas City Cardiomyopathy Questionnaire-Overall Summary score (KCCQ-OS) respectively. At month 30, the LS mean difference (95% CI) in change from baseline in 6MWD was 40 [21, 58] meters ($p < 0.0001$) and change from baseline in KCCQ-OS was 10 [6, 14] points ($p < 0.0001$).

There was a higher frequency of gastrointestinal (GI) adverse reactions such as diarrhea 11.6% versus 7.6% and upper abdominal pain 5.5% versus 1.4% in the acoramidis versus placebo group, respectively. The majority of these GI adverse reactions were categorized as mild and resolved without drug discontinuation.

A similar proportion of acoramidis-treated and placebo-treated participants discontinued study drug because of an adverse event (9.3% and 8.5%, respectively).

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of acoramidis (Attruby) **meets the definition of medical necessity** for members meeting **ALL** of the following criteria:

1. Diagnosis of cardiomyopathy due to hereditary transthyretin amyloidosis (hATTR) OR wild type transthyretin amyloidosis (ATTRwt) – documentation from the medical record must be provided

2. Past medical history of heart failure (HF) with at least 1 prior hospitalization for HF or clinical evidence of HF (without hospitalization) manifested by signs or symptoms of volume overload or elevated intracardiac pressures (e.g., elevated jugular venous pressure, shortness of breath or signs of pulmonary congestion on x-ray or auscultation, peripheral edema) that required/requires treatment with a diuretic for improvement) – documentation from the medical record must be provided
3. Left ventricular wall (interventricular septum or left ventricular posterior wall) thickness is equal to or greater than 12 mm – echocardiogram results must be provided
4. One of the following:
    a. Presence of amyloid deposits in biopsy tissue – laboratory documentation must be provided
    b. Presence of a variant TTR genotype and/or TTR precursor protein identification by immunohistochemistry, scintigraphy, or mass spectrometry – laboratory documentation must be provided
5. New York Heart Association (NYHA) classification of I, II, or III – documentation from the medical record must be provided
6. No evidence of primary (light chain) amyloidosis
7. None of the following clinical situations apply:
    a. Prior liver transplantation
    b. Prior heart transplantation
    c. Implanted cardiac mechanical assist device
8. Use will not be in combination with ANY of the following:
    a. Inotersen (Tegsedi)
    b. Patisiran (Onpattro)
    c. Tafamidis (Vyndamax, Vyndaqel)
9. Acoramidis is prescribed by (or in consultation with) a cardiologist, neurologist, geneticist, or physician specializing in the treatment of amyloidosis
10. Dose does not exceed 712 mg twice daily (4 tablets/day)

Approval duration: 6 months

Continuation of acoramidis (Attruby) meets the definition of **medical necessity** for members meeting the following criteria:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for treatment of cardiomyopathy due to either hereditary ATTR (hATTR) or wild type ATTR (ATTRwt) OR the member has previously met all indication-specific criteria
2. Member demonstrates a clinically meaningful beneficial response to treatment with acoramidis compared to baseline – documentation from the medical record must be provided
3. Use will not be in combination with ANY of the following:

a. Inotersen (Tegsedi)

b. Patisiran (Onpattro)

c. Tafamidis (Vyndamax, Vyndaqel)

4. Acoramidis is prescribed by (or in consultation with) a cardiologist, neurologist, geneticist, or physician specializing in the treatment of amyloidosis
5. Dose does not exceed 712 mg twice daily (4 tablets/day)

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

- Tablets: 356 mg acoramidis
- 712 mg twice daily

PRECAUTIONS:

None

BILLING/CODING INFORMATION:

HCPCS Coding

J8499	Prescription drug, oral, non-chemotherapeutic, Not Otherwise Specified

ICD-10 Diagnosis Codes That Support Medical Necessity

E85.1	Neuropathic heredofamilial amyloidosis

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date. [Change information as required]

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

None

RELATED GUIDELINES:

Inotersen (Tegsedi), 09-J2000-70

Patisiran (Onpattro), 09-J3000-16

Tafamidis (Vyndamax), Tafamidis Meglumine (Vyndaqel), 09-J3000-41

OTHER:

None

REFERENCES:

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2. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2025 [cited 2/1/25]. Available from: http://www.clinicalpharmacology.com/.
3. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 2/1/25]. Available from: http://clinicaltrials.gov/.
4. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2/1/25].
5. Gillmore JD, Judge DP, Cappelli F, et al. Efficacy and Safety of Acoramidis in Transthyretin Amyloid Cardiomyopathy. N Engl J Med 2024; 390:132-142.
6. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2025 [cited 2/1/25]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 02/12/25.

GUIDELINE UPDATE INFORMATION:

04/01/25	New Medical Coverage Guideline.