LOUISIANA BLUE

tafamidis (Vyndamax™)

Policy # 00694
Original Effective Date: 10/09/2019
Current Effective Date: 12/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Transthyretin silencers for the treatment of transthyretin-mediated amyloidosis in adult patients is addressed separately in medical policy 00670.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider tafamidis (Vyndamax™)‡ for the treatment of the cardiomyopathy of transthyretin-mediated amyloidosis (ATTR) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for tafamidis (Vyndamax) when the following criteria are met:

- **Initial:**
  - Patient has a diagnosis of cardiomyopathy of wild-type or hereditary transthyretin amyloidosis (ATTR); AND
  - Diagnosis is confirmed by ONE of the following:
    - A technetium pyrophosphate scan (i.e. nuclear scintigraphy); OR
    - Amyloid deposits identified on cardiac biopsy; AND
  - Patient is greater than or equal to 18 years of age; AND
  - Diagnostic cardiac imaging (e.g., echocardiogram, cardiac magnetic resonance imaging) has demonstrated cardiac involvement (e.g., increased thickness of the ventricular wall or interventricular septum); AND
  - Patient has New York Heart Association class I, II, or III heart failure; AND
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
  - Other forms of amyloidosis (e.g., light chain amyloidosis) have been ruled out; AND
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

  - Patient has NOT received a liver transplant; AND
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
  - Requested drug will NOT be used in combination with patisiran (Onpattro™)‡, eplontersen (Wainua™)‡, vutrisiran (Amvuttra™)‡, or acoramidis (Attruby™)‡
- **Continuation:**
  - Patient has received an initial authorization for the requested drug; AND
  - Patient does NOT have New York Heart Association class IV heart failure; AND
    *(Note: This criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
  - Patient has NOT received a liver transplant; AND
    *(Note: This criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
  - Requested drug will NOT be used in combination with patisiran (Onpattro), eplontersen (Wainua), vutrisiran (Amvuttra), or acoramidis (Attruby).

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of tafamidis (Vyndamax) when the patient has New York Heart Association class IV heart failure, has another form of amyloidosis, or has received a liver transplant to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of tafamidis (Vyndamax) when the patient selection criteria are not met (except for those denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Vyndaqel and Vyndamax are two formulations of the tetramer stabilizer, tafamidis, and are each indicated to reduce cardiovascular mortality and cardiovascular-related hospitalization in adults with cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis (ATTR-CM). Vyndaqel was the first of these products to launch and should be dosed as 80 mg (four 20 mg capsules) once daily. Vyndamax is an alternative formulation of tafamidis that was developed to allow for ease of dosing. The dose of Vyndamax is 1 capsule (61 mg) daily, which is bioequivalent to 80 mg of Vyndaqel. In 2025, Pfizer discontinued production of Vyndaqel. Although tafamidis is approved in the United States for the treatment of the cardiomyopathy associated with hereditary or wild-type transthyretin mediated amyloidosis (ATTR). Vyndaqel is approved in Europe for the treatment of the polyneuropathy of ATTR, an indication that the FDA declined to approve in 2012.

Clinical trials of tafamidis for cardiomyopathy excluded patients with a history of liver transplantation, New York Heart Association (NYHA) class IV heart failure, and other forms of amyloidosis (e.g., light-chain amyloidosis).

The TTR protein is primarily produced in the liver and circulates as a stable tetramer, transporting vitamin A and thyroxine throughout the body. With aging or in the setting of a mutation of the TTR gene, the stability of the TTR tetramer is altered, resulting in misfolding of the TTR protein. This leads to accumulation of amyloid in organs and tissues, causing symptoms based on the organ(s) involved. The most prominent symptoms are often those of cardiomyopathy or polyneuropathy (ATTR-CM or ATTR-PN). In ATTR-CM, amyloid deposits in cardiac tissue cause a weakening and/or stiffening of the heart. Although the clinical course varies, patients typically exhibit heart failure with preserved ejection fraction, but some patients may present with right-sided heart failure, atrial fibrillation, bundle branch block and complete heart block, angina, or cardiogenic shock. In ATTR-PN, neurologic symptoms include severe sensorimotor disturbances (loss of sensation, pain, muscle weakness, and loss of ambulation) and autonomic dysfunction resulting in orthostatic hypotension, diarrhea, impotence, and bladder disturbances. Patients may also present with a mixed phenotype and exhibit signs of both neuropathy and cardiomyopathy. This condition is progressive, debilitating, and life-threatening and may go unrecognized and result in late-stage diagnosis.

Management of ATTR-CM has historically been via standard therapies for heart failure such as diuretics, beta-blockers, mineralocorticoid receptor antagonists, and sodium-glucose cotransporter-2 inhibitors. Currently, there are two classes of disease modifying drugs available to treat the condition. Tafamidis is a stabilizer of TTR tetramers and vutrisiran (Amvuttra) is a TTR silencer approved for the treatment of ATTR-CM. These therapies have not been compared head-to-head and differences in clinical trial design make it difficult to compare efficacy and safety between products. The treatment landscape for this disease will continue to evolve as real-world evidence becomes available.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Vyndaqel and Vyndamax were approved in May 2019 for the treatment of the cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis in adults to reduce cardiovascular mortality and cardiovascular-related hospitalization. Pfizer discontinued Vyndaqel at the end of 2025.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Efficacy of tafamidis was demonstrated in a multicenter, international, randomized, double-blind, placebo-controlled study in 441 patients with wild type or hereditary ATTR-CM. Patients were randomized in a 1:2:2 ratio to receive Vyndaqel 20 mg (n = 88), Vyndaqel 80 mg (administered as four 20-mg Vyndaqel capsules) (n = 176), or matching placebo (n = 177) once daily for 30 months, in addition to standard of care (e.g., diuretics). Treatment assignment was stratified by the presence or absence of a variant TTR genotype as well as baseline disease severity (New York Heart Association Class). Transplant patients were excluded from this study.

The primary analysis used a hierarchical combination applying the method of Finkelstein-Schoenfeld (F-S) to all-cause mortality and frequency of cardiovascular-related hospitalizations, which was defined as the number of times a subject was hospitalized for cardiovascular-related morbidity. The method compared each patient to every other patient within each stratum in a pair-wise manner that proceeded in a hierarchical fashion using all-cause mortality followed by frequency of cardiovascular-related hospitalizations when patients could not be differentiated based on mortality. This analysis demonstrated a significant reduction (p = 0.0006) in all-cause mortality and frequency of cardiovascular-related hospitalizations in the pooled Vyndaqel 20 mg and 80 mg groups versus placebo. In the pooled Vyndaqel group, 70.5% of subjects were alive at month 30 compared to 57.1% of subjects in the placebo group. In addition, those alive in the pooled Vyndaqel group had an average of 0.297 cardiovascular-related hospitalizations compared to 0.455 in the placebo group.

Efficacy and safety of Vyndamax are based on pharmacokinetic studies demonstrating equivalence of Vyndamax 61 mg to Vyndaqel 80 mg (administered as four 20 mg capsules).

References

1. Vyndaqel and Vyndamax [package insert]. Pfizer Inc. New York, NY. Updated January 2025.
2. Vyndaqel and Vyndamax Drug Evaluation. Express Scripts. Updated May 2019.
3. Amvuttra (vutrisiran) New Drug Review. IPD Analytics June 2022.

Policy History

Original Effective Date: 10/09/2019
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10/03/2019	Medical Policy Committee review
10/09/2019	Medical Policy Implementation Committee approval. New policy.
10/01/2020	Medical Policy Committee review
10/07/2020	Medical Policy Implementation Committee approval. No change to coverage.
10/07/2021	Medical Policy Committee review
10/13/2021	Medical Policy Implementation Committee approval. No change to coverage.
10/06/2022	Medical Policy Committee review
10/11/2022	Medical Policy Implementation Committee approval. No change to coverage.
10/05/2023	Medical Policy Committee review
10/11/2023	Medical Policy Implementation Committee approval. No change to coverage.

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10/03/2024	Medical Policy Committee review
10/08/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/06/2025	Medical Policy Committee review
11/12/2025	Medical Policy Implementation Committee approval. Removed Vyndaqel from the policy due to its removal from the market. Added reference to new product, Attruby, and new indication for Amvuttra to criteria and background information. Removed reference to obsolete product, Tegsedi. Title changed from "tafamidis Products (Vyndaqel, (Vyndamax)" to "tafamidis (Vyndamax™)".

Next Scheduled Review Date: 11/2026

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.