Drug Coverage Policy

Effective Date 3/1/2026
Coverage Policy Number.....IP0149
Policy Title.....Tafamidis Products

Amyloidosis - Tafamidis Products

- Vyndaqel (tafamidis meglumine capsules – Pfizer)
- Vyndamax (tafamidis capsules – Pfizer)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Vyndaqel and Vyndamax are selective stabilizers of transthyretin (TTR) indicated for the treatment of the **cardiomyopathy of wild-type or hereditary TTR-mediated amyloidosis (ATTR-CM)** to reduce cardiovascular mortality and cardiovascular-related hospitalization in adults.[1] Studies excluded patients with New York Heart Association class IV disease.[2]

Disease Overview
In ATTR-CM, there is misfolding of the TTR protein resulting in accumulation of amyloid in the heart causing thickening of both ventricles.[2-8] ATTR-CM may be suspected following cardiac imaging (e.g., echocardiogram, cardiac magnetic imaging). Subsequent testing (e.g., scintigraphy or biopsy) confirms the diagnosis of ATTR-CM. Endomyocardial biopsy confirms the diagnosis of ATTR-CM.[8] Biopsy can confirm if ATTR-CM is due to a hereditary mutant variant of TTR vs. an acquired wild-type variant. In patients with confirmed cardiac amyloidosis, TTR gene sequencing aids in treatment decisions and is necessary for genetic counseling in relatives of patients with a TTR variant.[7] Although many mutations have been identified, mutation of V122I is the most common in the US.[2-6] This mutation is present in 3% to 4% of African Americans and is associated with amyloid cardiomyopathy. Vyndaqel and Vyndamax bind to TTR at the thyroxine binding sites and stabilize the tetramer. This slows dissociation into monomers, which is the rate-limiting step in the amyloidogenic process.[1]

Guidelines
The American Heart Association (AHA) scientific statement for the evolving diagnosis and management of cardiac amyloidosis (2020) recognizes tafamidis as a treatment for ATTR-CM.[7] They note that the benefit of tafamidis has not been observed in patients with NYHA class IV symptoms. Additionally, although combination use of tafamidis with Onpattro® (patisiran lipid complex intravenous infusion) or Tegsedi® (inotersen subcutaneous injection) is appealing to target both TTR silencing and stabilization for the remaining synthesized protein, this approach lacks data and may be cost-prohibitive. Tafamidis should generally be considered the agent of choice in ATTR-CM in patients with reasonable expected survival according to a position statement of the European Society of Cardiology (ESC) working group on myocardial and pericardial disease (2021).[8] The working group notes that tafamidis is the only drug that has shown efficacy in a randomized trial in patients with ATTR-CM and should be considered in patients with reasonable expected survival. The American College of Cardiology (ACC) expert consensus decision pathway on comprehensive multidisciplinary care for patients with cardiac amyloidosis (2023) make similar comments and recommendations to the AHA and ESC regarding tafamidis.[10]

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for benefit coverage of tafamidis products (Vyndaqel and Vyndamax). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with tafamidis products (Vyndaqel and Vyndamax) as well as the monitoring required for adverse events and long-term efficacy, initial approval requires the agent to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, and/or other information. All documentation must include patient-specific identifying information.

Tafamidis products (Vyndaqel and Vyndamax) are considered medically necessary when the following are met:

FDA-Approved Indication

1. **Cardiomyopathy of Wild-Type or Hereditary Transthyretin Amyloidosis.** Approve for 1 year if the patient meets **ALL** of the following criteria (A, B, C, D and E):
   Note: Variant Transthyretin Amyloidosis is also known as Hereditary Transthyretin Amyloidosis.
   A. Individual is ≥ 18 years of age ; AND
   B. The diagnosis confirmed by **ONE** of the following (i, ii, or iii):
      i. A technetium pyrophosphate scan (i.e., nuclear scintigraphy) **[documentation required]**; OR
      ii. A tissue biopsy with confirmatory transthyretin (TTR) amyloid typing by mass spectrometry, immunoelectron microscopy or immunohistochemistry **[documentation required]**; OR
      iii. Patient had genetic testing which identified a transthyretin (TTR) pathogenic variant**[documentation required]**; AND
      Note: Examples of TTR variants include Val122Ile variant and Thr60Ala variant. If the patient has wild-type amyloidosis, this is **not** a TTR pathogenic variant.
   C. Diagnostic cardiac imaging has demonstrated cardiac involvement; AND
      Note: Examples of cardiac imaging include echocardiogram and cardiac magnetic imaging. Examples of cardiac involvement on imaging include increased thickness of the ventricular wall or interventricular septum.
   D. Patient has heart failure, but does **not** have New York Heart Association class IV disease; AND
   E. The medication is being prescribed by or in consultation with a cardiologist or a physician who specializes in the treatment of amyloidosis

Conditions Not Covered

Tafamidis products (Vyndaqel and Vyndamax) for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concurrent use with other medications indicated for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis or transthyretin-mediated amyloidosis-cardiomyopathy (e.g., Amvuttra [vutrisiran subcutaneous injection], Attruby [acoramidis tablets], Onpattro [patisiran lipid complex intravenous infusion], Tegsedi [inotersen subcutaneous injection], or Wainua [eplontersen subcutaneous injection]).**
   The requested medication should not be administered in combination with other medications indicated for polyneuropathy of hereditary transthyretin-mediated amyloidosis or transthyretin-mediated amyloidosis-cardiomyopathy. Combination therapy is generally not recommended due to a lack of controlled clinical trial data supporting additive efficacy.

2. **Concurrent Use of Vyndaqel and Vyndamax.** There are no data available to support concomitant use.

3. **Polyneuropathy of Hereditary Transthyretin–Mediated Amyloidosis (hATTR).** Neither Vyndaqel nor Vyndamax are indicated for treatment of symptoms of polyneuropathy associated with hATTR.[1]
   Note: For patients with hATTR and cardiomyopathy or mixed phenotype (concurrent cardiomyopathy and polyneuropathy), refer to FDA-Approved Indication, above.

References

1. Vyndaqel and Vyndamax capsules [prescribing information]. New York, NY: Pfizer; October 2023.
2. Maurer MS, Schwartz JH, Gundapaneni B, et al. Tafamidis treatment for patients with transthyretin amyloid cardiomyopathy. *N Engl J Med*. 2018;379(11):1007-1016.
3. Maurer MS, Elliott P, Merlini G, et al. Design and rationale of the Phase 3 ATTR-ACT clinical trial (tafamidis in transthyretin cardiomyopathy clinical trial). *Circ Heart Fail*. 2017;10(6).
4. Maurer MS, Bokhari S, Damy T, et al. Expert consensus recommendations for the suspicion and diagnosis of transthyretin cardiac amyloidosis. *Circ Heart Fail.* 2019 Sep;12(9):e006075.
5. Donnelly JP, Hanna M. Cardiac amyloidosis: an update on diagnosis and treatment. *Cleve Clin J Med*. 2017;84(12 Suppl 3):12-26.
6. Siddiqi OK, Ruberg FL. Cardiac amyloidosis: an update on pathophysiology, diagnosis, and treatment. *Trends Cardiovasc Med*. 2018;28(1):10-21.
7. Lin H, Merkel M, Hale C, Marantz JL. Experience of patisiran with transthyretin stabilizers in patients with hereditary transthyretin-mediated amyloidosis. *Neurodegener Dis Manag*. 2020;10(5):289-300.
8. Kittleson MM, Maurer MS, Ambardekar AV, et al; on behalf of the American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology. AHA scientific statement: cardiac amyloidosis: evolving diagnosis and management. *Circulation.* 2020;142:e7-e22.
9. Garcia-Pavia P, Rapezzi C, Adler Y, et al. Diagnosis and treatment of cardiac amyloidosis: a position statement of the ESC working group on myocardial and pericardial disease. *Eur Heart J.* 2021;42:1554-1568.
10. Kittleson M, Ruberg FL, Ambardekar AV, et al. A report of the American College of Cardiology Solution Set Oversight Committee. 2023 ACC expert consensus decision pathway on comprehensive multidisciplinary care for the patient with cardiac amyloidosis. *JACC*. 2023;81(11):1076-1126.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Added "<u>Documentation</u>**: Documentation is required where noted in the criteria. Documentation may include, but not limited to, chart notes, laboratory tests, medical test results, genetic test results, claims records, and/or other information." **Cardiomyopathy of Wild-Type or Hereditary Transthyretin Amyloidosis.** The criterion Amyloid deposits are identified on cardiac biopsy was changed to A tissue biopsy with confirmatory TTR amyloid typing by mass spectrometry, immunoelectron microscopy or immunohistochemistry. For diagnosis confirmed by genetic testing, rephrased the term "mutation" to "pathogenic variant." **Conditions Not Covered** Concurrent use with other medications indicated for polyneuropathy of hereditary transthyretin-mediated amyloidosis or transthyretin-mediated amyloidosis-cardiomyopathy (e.g., Amvuttra (vutrisiran subcutaneous injection), Attruby	3/1/2025

	(acoramidis tablets), Onpattro (patisiran lipid complex intravenous infusion), Tegsedi (inotersen subcutaneous injection), or Wainua [eplontersen subcutaneous injection]) was changed to as listed (previously Concomitant Use With Amvuttra (vutrisiran subcutaneous injection), Onpattro (patisiran lipid complex intravenous infusion), Tegsedi (inotersen subcutaneous injection), or Wainua [eplontersen subcutaneous injection]).	
Annual Revision	**Cardiomyopathy of Wild-Type or Hereditary Transthyretin Amyloidosis.** For diagnosis confirmed by genetic testing, rephrased the term "mutation" to "pathogenic variant."	3/1/2026

The policy effective date is in force until updated or retired.