Clinical Policy: Tafamidis (Vyndaqel, Vyndamax)

Reference Number: PA.CP.PHAR.432
Effective Date: 01/2020
Last Review Date: 04/2025

Description
Tafamidis meglumine (Vyndaqel®) and tafamidis (Vyndamax™) are transthyretin stabilizers.

FDA Approved Indication(s)
Vyndaqel and Vyndamax are indicated for the treatment of the cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular mortality and cardiovascular-related hospitalization.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Vyndaqel and Vyndamax are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Transthyretin Amyloid Cardiomyopathy (must meet all)**:**

1. Diagnosis of cardiomyopathy caused by ATTR;
2. Prescribed by or in consultation with a cardiologist;
3. Age ≥ 18 years;
4. Diagnosis is supported by one of the following (a or b):
   a. Tissue biopsy amyloid protein is identified as transthyretin via mass spectrometry or immunohistochemistry, and (i or ii):
      i. Tissue biopsy is of endomyocardial origin;
      ii. Tissue biopsy is of extra-cardiac origin and echocardiography (Echo), cardiac magnetic resonance imaging (CMR), or positron emission tomography (PET) findings are consistent with cardiac amyloidosis;
   b. Member meets all of the following (i, ii, and iii):
      i. Echo, CMR, or PET findings are consistent with cardiac amyloidosis;
      ii. Cardiac uptake is Grade 2 or 3 on a radionuclide scan utilizing one of the following radiotracers (1, 2, or 3):
         1) 99m technetium (Tc)-labeled 3,3-diphosphono-1,2-propanodicarboxylic acid (DPD);
         2) 99mTc-labeled pyrophosphate (PYP);
         3) 99mTc-labeled hydroxymethylene diphosphonate (HMDP);
      iii. Each of the following laboratory tests is negative for monoclonal protein (1, 2, and 3):
         1) Serum kappa/lambda free light chain ratio analysis;
         2) Serum protein immunofixation;
         3) Urine protein immunofixation;
5. Member has heart failure of New York Heart Association (NHYA) Class I, II, or III;

6. Member has one of the following (a or b):
   a. At least 1 prior hospitalization for heart failure;
   b. History of clinical evidence of heart failure (i.e., signs and symptoms, see *Appendix D*);
7. Member has not had a liver transplant;
8. Vyndaqel/Vyndamax is not prescribed concurrently with Attruby™ or Onpattro® ;
9. If member is currently receiving treatment with Amvuttra™ and request is for concurrent use with Vyndaqel/Vyndamax (i.e., not switching from one agent to another), provider must submit evidence of both of the following (a and b):
   a. Member has experienced and maintained positive response to Amvuttra monotherapy following at least 6 months of monotherapy;
   b. Despite Amvuttra monotherapy, member continues to require cardiac-related hospitalization;
10. Dose does not exceed either of the following (a or b):
    a. Vyndaqel: 80 mg (4 capsules) per day;
    b. Vyndamax: 61 mg (1 capsule) per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Transthyretin Amyloid Cardiomyopathy (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy, including but not limited to improvement or stabilization in any of the following parameters:
   a. Walking ability;
   b. Nutrition (e.g., body mass index);
   c. Cardiac related hospitalization;
   d. Cardiac procedures or laboratory tests (e.g., Holter monitoring, echocardiography, electrocardiogram, plasma BNP or NT-proBNP, serum troponin);
3. Vyndaqel/Vyndamax is not prescribed concurrently with Attruby or Onpattro;
4. Dose does not exceed either of the following (a or b):
   a. Vyndaqel: 80 mg (4 capsules) per day;
   b. Vyndamax: 61 mg (1 capsule) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ATTR-CM: cardiomyopathy of transthyretin-mediated amyloidosis
CMR: cardiac magnetic resonance imaging
DPD: 99Tc-labeled 3,3-diphosphono-1,2-propanodicarboxylic acid
Echo: echocardiography
FDA: Food and Drug Administration
HF: heart failure
HMDP: 99mTc-labeled hydroxymethylene diphosphonate
NHYA: New York Heart Association
PET: positron emission tomography
PYP: 99mTc-labeled pyrophosphate
Tc: technetium

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- There is no evidence supporting the safety and efficacy of concurrent use of Attruby or Onpattro with Vyndaqel/Vyndamax.
    - In the APOLLO Phase II open-label extension in 27 patients treated with Onpattro (13 treated concomitantly with Onpattro and tafamidis), transthyretin reduction was similar over 24 months, regardless of concomitant transthyretin stabilizers (i.e., tafamadis, diflunisal).
- While signs and symptoms of advanced heart failure are variable, common manifestations of advanced hear failure include exercise intolerance, unintentional weight loss, refractory volume overload, recurrent ventricular arrhythmias, as well as hypotension and signs of inadequate perfusion (e.g., low or narrowed pulse pressure, cool extremities, and mental status changes). Laboratory testing that may reveal signs of advanced heart failure includes indications of poor or worsening renal function, hyponatremia, hypoalbuminemia, congestive hepatopathy, elevated serum natriuretic peptide levels. Pulmonary edema, pleural effusions, and/or pulmonary vascular congestion on chest radiograph are also suggestive of advanced heart failure.

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Tafamidis meglumine (Vyndaqel)	80 mg (4 capsules) PO QD	80 mg/day
Tafamidis (Vyndamax)	61 mg (1 capsule) PO QD	61 mg/day

VI. Product Availability

Drug Name	Availability
Tafamidis (Vyndaqel)	Capsules: 20 mg
Tafamidis (Vyndamax)	Capsules: 61 mg

VII. References

1. Vyndaqel, Vyndamax Prescribing Information. New York, NY; Pfizer, Inc.; October 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/211996s000,212161s000lbl.pdf. Accessed May 9, 2024.
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. Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet Journal of Rare Diseases. 2013; 8:31.
4. Gillmore JD, Maurer MS, Falk RH, et al. Nonbiopsy diagnosis of cardiac transthyretin amyloidosis. Circulation. 2016;133(24):2404. Epub 2016 Apr 22.
5. Dorbala S, Ando Y, Bokhari S, et al. ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI expert consensus recommendations for multimodality imaging in cardiac amyloidosis: Part 1 of 2 - Evidence base and standardized methods of imaging. J Cardiac Failure; 2019: 24(11): e2-e39.
6. Dorbala S, Ando Y, Bokhari S, et al. ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI expert consensus recommendations for multimodality imaging in cardiac amyloidosis: Part 2 of 2-Diagnostic criteria and appropriate utilization. Journal of Cardiac Failure; 2019: 25(11): 854-865.
7. Witteles RM, Bokhari S, Damy T, et al. Screening for transthyretin amyloid cardiomyopathy in everyday practice. JACC, August 2019; 7(8): 709-16.
8. Kittleson MM, Maurer MS, Ambardekar AV, et al. Cardiac Amyloidosis: Evolving Diagnosis and Management: A Scientific Statement From the American Heart Association. Circulation; 2020 July: 142 (1): e7-e22.
9. Lin H, Merkel M, Hale C, et al. Experience of patisiran with transthyretin stabilizers in patients with hereditary transthyretin-mediated amyloidosis. Neurodegener Dis Manag. 2020;10(5):289-300.
10. Fontana M, Berk JL, Gillmore JD, et al.; HELIOS-B Trial Investigators and Collaborators. Vutrisiran in patients with transthyretin amyloidosis with cardiomyopathy. N Engl J Med. 2025 Jan 2;392(1):33-44.

Reviews, Revisions, and Approvals	Date
Policy created	01/2020
3Q 2020 annual review: Cardiac scintigraphy added as a tissue biopsy alternative for ATTR-CM; references reviewed and updated.	07/2020
3Q 2021 annual review: no significant changes; references reviewed and updated.	07/2021

Reviews, Revisions, and Approvals	Date
3Q 2022 annual review: added requirement that Vyndaqel/Vyndamax is not prescribed concurrently with Onpattro and Tegsedi; references reviewed and updated.	07/2022
3Q 2023 annual review: added the following requirements per pivotal trial inclusion criteria and competitor analysis - member has heart failure of NHYA Class I, II, or III; and member has at least 1 prior hospitalization for heart failure or current (within the last 30 days) clinical evidence of heart failure; references reviewed and updated.	07/2023
3Q 2024 annual review: removed Tegsedi from criteria as agent will be discontinued September 2024 per Sobi manufacturer; revised Vyndaqel/Vyndamax is "not prescribed concurrently with Onpattro and Tegsedi" to "not prescribed concurrently with Onpattro and Amvuttra"; updated Appendix D by removing Tegsedi and adding Amuvttra supplemental information on concurrent use; references reviewed and updated.	07/2024
Removed Amvuttra from list of excluded agents for concurrent use per HELIOS-B study; added requirements to requests for concurrent use with Amvuttra, requiring positive but inadequate response to monotherapy; added Attruby to list of excluded agents for concurrent use in initial approval criteria and continued therapy.	04/2025