Clinical Policy: Tafamidis (Vyndaqel, Vyndamax)

Reference Number: CP.PHAR.432
Effective Date: 09.01.19
Last Review Date: 08.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 health plans affiliated with Centene Corporation® 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 ATTR-CM;
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 SPECT (Single Photon Emission Computed Exercise Tomography) 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. Current (within the last 30 days) clinical evidence of heart failure (e.g., exercise intolerance, unintentional weight loss, refractory volume overload, recurrent ventricular arrhythmias, hypotension and signs of inadequate perfusion [e.g., low, or narrowed pulse pressure, cool extremities, and mental status changes], 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: 12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

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
SPECT: Single Photon Emission Computed Exercise Tomography
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 meglumine (Vyndaqel)	Capsule: 20 mg
Tafamidis (Vyndamax)	Capsule: 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/2023/211996s002,212161s002lbl.pdf. Accessed April 14, 2026.
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.
11. Kittleson MM, Ambardekar AV, Cheng RK, et al. Transthyretin cardiac amyloidosis evaluation and management: 2025 ACC Concise Clinical Guidance. J Am Coll Cardiol. 2025 Oct 31:S0735-1097(25)07719-8. doi: 10.1016/j.jacc.2025.09.004.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Template changes applied to other diagnoses/indications and continued therapy section.	09.26.22	
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.	04.18.23	08.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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.	05.09.24	08.24
For initial approval criteria and continued therapy, added Attruby to list of excluded agents for concurrent use.	12.10.24	
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.	03.31.25	05.25
3Q 2025 annual review: no significant changes; references reviewed and updated.	05.23.25	08.25
3Q 2026 annual review: for diagnosis by cardiac uptake, specified radionucleotide scan should be SPECT per updated 2025 ACC Clinical Guidance; in initial approval criteria, added examples of heart failure from Appendix D; revised initial approval duration from 6 to 12 months; added ICHRA line of business; references reviewed and updated.	04.14.26	08.26

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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