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Subject: Tafamidis (Vyndamax), Tafamidis Meglumine (Vydnaqel)

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™).

Tafamidis (Vyndamax) and tafamidis meglumine (Vyndaqel), selective TTR stabilizers, were approved by the U.S. Food and Drug Administration (FDA) in May 2019 for use in the treatment of the

cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis in adults to reduce cardiovascular mortality and cardiovascular-related hospitalization.

The safety and efficacy of tafamidis were evaluation in a randomized, double-blind phase 3 trial (ATTR-ACT) of patients with transthyretin amyloid cardiomyopathy (n=441). Patients were randomized to receive 80 mg of tafamidis, 20 mg of tafamidis, or placebo for 30 months. The primary endpoint was all-cause mortality, followed by frequency of cardiovascular-related hospitalizations. Key secondary end points were the change from baseline to month 30 for the 6-minute walk test and the score on the Kansas City Cardiomyopathy Questionnaire–Overall Summary (KCCQ-OS), in which higher scores indicate better health status.

In the primary analysis, all-cause mortality and rates of cardiovascular-related hospitalizations were lower among the 264 patients who received tafamidis than among the 177 patients who received placebo (P<0.001). Tafamidis was associated with lower all-cause mortality than placebo (78 of 264 [29.5%] vs. 76 of 177 [42.9%]; hazard ratio, 0.70; 95% confidence interval [CI], 0.51 to 0.96) and a lower rate of cardiovascular-related hospitalizations, with a relative risk ratio of 0.68 (0.48 per year vs. 0.70 per year; 95% CI, 0.56 to 0.81). At month 30, tafamidis was also associated with a lower rate of decline in distance for the 6-minute walk test (P<0.001) and a lower rate of decline in KCCQ-OS score (P<0.001). The incidence and types of adverse events were similar in the two groups.

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.

NOTE: Attruby (ATTR-CM), Vyndamax (ATTR-CM), Vyndaqel (ATTR-CM), and Wainua (ATTR-PN) are the preferred products for ATTR-CM and ATTR-PN

Initiation of tafamidis (Vyndamax) and tafamidis meglumine (Vyndaqel) **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. Presence of a variant TTR genotype and/or TTR precursor protein identification by immunohistochemistry, scintigraphy, or mass spectrometry – laboratory documentation must be provided
3. New York Heart Association (NYHA) classification of I, II,or III – documentation from the medical record must be provided
4. None of the following clinical situations apply:
    a. Prior liver transplantation
    b. Prior heart transplantation

    c. Implanted cardiac mechanical assist device
5. Use will not be in combination with ANY of the following:
    a. Acoramidis (Attruby)
    b. Eplontersen (Wainua)
    c. Inotersen (Tegsedi)
    d. Patisiran (Onpattro)
    e. Vutrisiran (Amvuttra)
6. Tafamidis or tafamidis meglumine is prescribed by (or in consultation with) a cardiologist, neurologist, geneticist, or physician specializing in the treatment of amyloidosis
7. Dose does not exceed the following:
    a. Vyndaqel: 80 mg daily
    b. Vyndamax: 61 mg daily

Approval duration: 1 year

Continuation of tafamidis (Vyndamax) and tafamidis meglumine (Vyndaqel) **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 tafamidis compared to baseline – documentation from the medical record must be provided
3. Use will not be in combination with ANY of the following:
    a. Acoramidis (Attruby)
    b. Eplontersen (Wainua)
    c. Inotersen (Tegsedi)
    d. Patisiran (Onpattro)
    e. Vutrisiran (Amvuttra)
4. Tafamidis or tafamidis meglumine is prescribed by (or in consultation with) a cardiologist, neurologist, geneticist, or physician specializing in the treatment of amyloidosis
5. Dose does not exceed the following:
    a. Vyndaqel: 80 mg daily
    b. Vyndamax: 61 mg daily

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- The recommended dosage is either VYNDAQEL 80 mg (four 20-mg tafamidis meglumine capsules) orally once daily or VYNDAMAX 61 mg (one 61-mg tafamidis capsule) orally once daily.
- VYNDAMAX and VYNDAQEL are not substitutable on a per mg basis.
- The capsules should be swallowed whole and not crushed or cut.

Dose Adjustments

- None

Drug Availability

- Capsules: Tafamidis meglumine 20 mg and tafamidis 61 mg

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- None

Precautions/Warnings

- None

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

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

ICD-10 Diagnoses 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: BCBSF 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.

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

OTHER:

None

REFERENCES:

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4. 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.
5. Pfizer. Vyndamax, Vyndaqel (tafamidis) capsule. 2019 [cited 7/27/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=1b4121ee-a733-4456-a917-be2603477839
6. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2025 [cited 6/1/25]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the BCBSF Pharmacy Policy Committee on 02/11/26.

GUIDELINE UPDATE INFORMATION:

09/15/19	New Medical Coverage Guideline.
07/15/25	Review and revision to guideline; updated position statement and references
08/15/25	Review and revision to guideline; updated position statement and references
10/15/25	Revision to guideline; updated position statement
03/15/26	Retire; Merging MCGs 09-J3000-41, Tafamidis (Vyndamax, Vyndaqel) Oral, 09-J4000-77, Eplontersen (Wainua), 09-J3000-16 Patisiran (Onpattro™), 09-J4000-32 Vutrisiran (Amvuttra), and 09-J5000-11, Acoramidis (Attruby) to 09-J5000-50, Transthyretin Amyloidosis (ATTR).