



Policy Type: PA/SP

Pharmacy Coverage Policy: EOCCO064

Description

Tafamidis meglumine (Vyndaqel) and tafamidis (Vyndamax) are orally administered transthyretin stabilizers.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit	DDID
tafamidis meglumine (Vyndaqel)	20 mg capsules	Cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis	120 capsules/30 days	TBD
tafamidis (Vyndamax)	61 mg capsules		30 capsules/30 days	206614

Initial Evaluation*

* Tafamidis meglumine (Vyndaqel) and tafamidis (Vyndamax) is a medication used to treat transthyretin-mediated amyloidosis, a non-funded condition according to the Oregon Health Plan Prioritized List of Healthcare Services.

Amyloidosis falls under non covered line 650. Cardiomyopathy falls under covered line 99, but does not address cardiomyopathy due to amyloidosis. Alternatively code E85.82 applies to wild-type transthyretin-related (ATTR) amyloidosis which falls under covered lines 235 and 261. However these lines consist of acute lymphocytic leukemia and multiple myeloma.

If the condition becomes a covered line according to the Oregon Health Plan Prioritized List of Healthcare Services, the following applies:

- I. Tafamidis meglumine (Vyndaqel) and tafamidis (Vyndamax) may be considered medically necessary when the following criteria below are met:
 - A. Member 18 years or older; **AND**
 - B. Medication is prescribed by or in consultation with a neurologist or cardiologist; **AND**
 - C. Tafamidis meglumine (Vyndaqel) or tafamidis (Vyndamax) will not be used in combination with other agents for the treatment of transthyretin-mediated amyloidosis [i.e. inotersen (Tegsedi), patisiran (Onpattro)]; **AND**



- D. A diagnosis of **cardiomyopathy of wild type (ATTRwt-CM) or hereditary transthyretin-mediated amyloidosis (hATTR-CM)** when the following are met:
1. Confirmed transthyretin-mediated amyloidosis by one of the following:
 - i. Documented presence of amyloid deposit by biopsy; **OR**
 - ii. Presence of transthyretin precursor protein confirmed by scintigraphy (i.e. radiotracer 99m technetium pyrophosphate (99mTc-PYP))
- AND**
2. History of heart failure; **AND**
 3. Evidence of cardiac involvement by echocardiography with an end-diastolic interventricular septal wall thickness > 12 mm; **AND**
 4. New York Heart Association (NYHA) functional class I-III; **AND**
 5. No prior history of liver or heart transplantation
- II. Tafamidis meglumine (Vyndaqel) and tafamidis (Vyndamax) is considered not medically necessary when used for all other conditions, including but not limited to:
- A. Cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis in members with NYHA functional class IV
- III. Tafamidis meglumine (Vyndaqel) and tafamidis (Vyndamax) is considered investigational when used for all other conditions, including but not limited to:
- A. Polyneuropathy of hereditary transthyretin-mediated amyloidosis (ATTR-PN) or familial amyloid polyneuropathy (FAP)
 - B. Primary (light chain) amyloidosis

Renewal Evaluation

- I. Member has previously received treatment with tafamidis meglumine (Vyndaqel) or tafamidis (Vyndamax); **AND**
- II. Documentation that the patient has experienced a positive clinical response therapy (e.g., reduced cardiovascular hospitalizations, improved quality of life, slowing of disease progression, etc.); **AND**
- III. No prior history of liver or heart transplantation; **AND**
- IV. New York Heart Association (NYHA) functional class I-III; **AND**
- V. Tafamidis meglumine (Vyndaqel) or tafamidis (Vyndamax) will not be used in combination with other agents for the treatment of transthyretin-mediated amyloidosis [i.e. inotersen (Tegsedi), patisiran (Onpattro)].

Supporting Evidence



- I. Tafamidis meglumine (Vyndaqel) and tafamidis (Vyndamax) are transthyretin stabilizers FDA approved 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.
- II. Vyndamax (tafamidis) was developed for patient convenience. Vyndaqel (tafamidis meglumine) and Vyndamax (tafamidis) are not substitutable on a per-mg basis.
- III. Tafamidis meglumine (Vyndaqel) was studied in a phase 3, multicenter, international, randomized, double-blind, placebo-controlled study in 441 patients with wild type or hereditary ATTR-CM (ATTR-ACT trial). The trial met its primary endpoint, demonstrating a significant reduction ($p=0.0006$) in all-cause mortality and frequency of cardiovascular-related hospitalizations ($p<0.0001$) in the pre-specified pooled tafamidis meglumine (Vyndaqel) 20-mg and 80-mg groups versus placebo at 30 months. Tafamidis meglumine (Vyndaqel) also showed a lower rate of decline in distance for the 6-minute walk test and lower rate of decline in the Kansas City Cardiomyopathy Questionnaire Overall Summary score (KCCQ-OS). Of note, subgroup analysis of patients identified as NYHA class III at baseline did not show a reduction in all-cause mortality or cardiovascular related hospitalizations. In the NYHA class III patients, cardiovascular related hospitalizations were actually higher among patients receiving tafamidis meglumine (Vyndaqel) than those receiving placebo.
- IV. NYHA Classification - The Stages of Heart Failure:
 - Class I - No symptoms and no limitation in ordinary physical activity, e.g. shortness of breath when walking, climbing stairs etc.
 - Class II - Mild symptoms (mild shortness of breath and/or angina) and slight limitation during ordinary activity.
 - Class III - Marked limitation in activity due to symptoms. Less than ordinary physical activity causes fatigue, palpitation, dyspnea, or anginal pain. Comfortable at rest.
 - Class IV - Severe limitations. Inability to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency or of the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.
- V. Patients included in the pivotal trial had a history of heart failure, evidence of cardiac involvement by echocardiography with an end-diastolic interventricular septal wall thickness > 12 mm, and confirmed transthyretin-mediated amyloidosis by documented presence of amyloid deposit by biopsy and/or presence of transthyretin precursor protein confirmed by scintigraphy.
- VI. Nuclear scintigraphy is a newer, less invasive diagnostic method thought to improve the diagnosis rate of ATTR-CM. Though use of this diagnostic tool may be limited, due to the specialized nature of the protocol and the skill needed for interpretation of the results. There are two radiolabeled phosphonates that have been studied most in this setting, ^{99m}Tc -pyrophosphate (^{99m}Tc -PYP) in the US and ^{99m}Tc -3,3-diphosphono-1,2-propanodicarboxylic acid (^{99m}Tc -DPD) in Europe. In the US, the radiotracer 99m technetium pyrophosphate, or ^{99m}Tc -PYP,



is not FDA-approved for the diagnosis of ATTR-CM, but it is increasingly used by the medical community.

- VII. Patients were excluded if they had NYHA Class IV heart failure, primary amyloidosis, or a history of liver or heart transplantation.
- Primary amyloidosis was excluded as this diagnosis is considered emergent and entails a different treatment approach consisting of chemotherapy.
 - Before the availability of tafamidis the management of ATTR-CM consisted of symptomatic treatment of heart failure symptoms and liver and/or heart transplantation. Orthotopic liver transplant (OLT) is one of the most established, potentially curative treatment options for some patients with ATTR-CM, specifically patients with early-stage hATTR. Orthotopic heart transplant (OHT), alone or in combination with OLT, may be a therapeutic option for select patients with ATTR-CM.
 - Tafamidis meglumine (Vyndaqel) is designed to target the underlying disease process in ATTR-CM through inhibition of the TTR tetramer dissociation. This forms the rationale for the use of tafamidis meglumine to slow disease progression. The progressive nature of the disease underscores the importance of early diagnosis and suggests tafamidis meglumine treatment may be most beneficial when initiated in early stages of the disease when heart failure is less severe and may be more easily reversed compared with later stages. Disease-modifying treatments, such as tafamidis meglumine (Vyndaqel) may be less effective once amyloid deposition has caused irreversible organ damage.
- VIII. Tafamidis meglumine (Vyndaqel) was studied as monotherapy. There is no data on the use of combination therapy with other medications indicated for different types of amyloid disease.
- IX. Within the pivotal trial results, a greater proportion of patients in the tafamidis meglumine group either improved upon or remained at their respective NYHA baseline classification compared with patients in the placebo group.

Investigational or Not Medically Necessary Uses

- I. Cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis in members with NYHA functional class IV
- A. In the ATTR-ACT trial, patients with NYHA Class IV were excluded from the pivotal trial. The progressive nature of the disease underscores the importance of early diagnosis and suggests tafamidis meglumine treatment may be most beneficial when initiated in early stages of the disease when heart failure is less severe and may be more easily reversed compared with later stages. Disease-modifying treatments, such as tafamidis meglumine (Vyndaqel) may be less effective once amyloid deposition has caused irreversible organ damage.



- II. Polyneuropathy of hereditary transthyretin-mediated amyloidosis or familial amyloid polyneuropathy (FAP)
 - A. Coelho et al. 2012 reported no significant changes in patients with early-stage V30M transthyretin familial amyloid polyneuropathy (TTR-FAP) as coprimary endpoints were not met in the ITT population.
 - B. The US FDA did not approve tafamidis meglumine (Vyndaqel) use in FAP during a filing in 2012, due to limited efficacy data. The agency requested the completion of a second efficacy study to establish substantial evidence of effectiveness prior to an approval.
- III. Primary (light chain) amyloidosis
 - A. In the pivotal trial (ATTR-ACT), patients with primary amyloidosis were excluded. Primary amyloidosis is caused by a bone marrow disorder. Treatment consists of chemotherapy or bone marrow transplant.

References

1. Vyndamax (tafamidis) [prescribing information]. New York, NY: Pfizer Labs; May 2019.
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Policy Implementation/Update:

Date Created	May 2019
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 EASTERN OREGON
 COORDINATED CARE
 ORGANIZATION
EOCCO POLICY



Date Effective	August 2019
Last Updated	
Last Reviewed	

Action and Summary of Changes	Date