

## PRIOR AUTHORIZATION POLICY

- POLICY:** Amyloidosis – Tafamidis Products
- Vyndaqel (tafamidis meglumine capsules – Pfizer)
  - Vyndamax (tafamidis capsules – Pfizer)

**REVIEW DATE:** 10/28/2020

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### OVERVIEW

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

### 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.<sup>2-6</sup> 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 is almost 100% sensitive for diagnosis of transthyretin amyloidosis and is the gold standard for diagnosis. 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. Although many mutations have been identified, mutation of V122I is the most common in the US. 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.<sup>1</sup>

### Guidelines

The Cleveland Clinic amyloidosis center has an update on the diagnosis and treatment of cardiac amyloidosis (2017), published prior to approval of Vyndaqel and Vyndamax in the US.<sup>5</sup> Treatment of ATTR-CM focuses on management of cardiac symptoms and treating the underlying disease. Liver transplantation is a potential treatment for the hereditary mutant variant of TTR but not for wild-type disease. Heart transplantation (sometimes in combination with liver transplantation) is a treatment option for patients with both wild-type and hereditary variants of ATTR-CM. Although limited data are available, the following three pharmacologic classes were discussed for treatment or future treatment of the underlying ATTR-CM disease process: 1) agents that block TTR synthesis; 2) therapies that stabilize the TTR tetramer (e.g., tafamidis, diflunisal); and 3) agents that disrupt and clear the ATTR amyloid fibril (e.g., doxycycline).

### POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of tafamidis products (Vyndaqel and Vyndamax). Because of the specialized skills required for evaluation and diagnosis of patients treated with 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. All approvals are provided for the duration noted below.

**Automation:** None.

### **RECOMMENDED AUTHORIZATION CRITERIA**

Coverage of Vyndaqel and Vyndamax is recommended in those who meet the following criteria:

#### **FDA-Approved Indications**

- 1. Cardiomyopathy of Wild-Type or Hereditary Transthyretin Amyloidosis.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
  - A)** Patient is 18 years of age or older; AND
  - B)** The diagnosis was confirmed by one of the following (i, ii, or iii):
    - i.** A technetium pyrophosphate scan (i.e., nuclear scintigraphy); OR
    - ii.** Amyloid deposits are identified on cardiac biopsy; OR
    - iii.** Patient had genetic testing which, according to the prescriber, identified a transthyretin (TTR) mutation; AND  
Note: Examples of TTR mutations include Val122Ile mutation and Thr60Ala mutation. If the patient has wild-type amyloidosis, this is **not** a TTR mutation.
  - 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 prescribed by or in consultation with a cardiologist or a physician who specializes in the treatment of amyloidosis.

#### **CONDITIONS NOT RECOMMENDED FOR APPROVAL**

Coverage of Tafamidis products (Vyndaqel and Vyndamax) is not recommended in the following situations:

- 1. Concomitant Use With Onpattro (patisiran lipid complex intravenous infusion) or Tegsedi (inotersen subcutaneous injection).** There are no data supporting the safety and efficacy of concurrent use with Vyndaqel/Vyndamax. The Vyndaqel/Vyndamax pivotal trial, which took place prior when Onpattro and Tegsedi were under investigation for amyloidosis, did not include patients who were taking investigational drugs. The pivotal trials for Onpattro and Tegsedi did not allow concurrent use of tetramer stabilizers (e.g., tafamidis, diflunisal). A Phase II open-label extension study, included 13 patients who were treated with concomitantly with Onpattro and tafamidis.<sup>7</sup> Following 24 months of treatment, there was not significant difference in the median serum TTR percent change from baseline with concomitant Onpattro and tafamidis (-80%) vs. Onpattro monotherapy (-88%).
- 2. Concurrent Use of Vyndaqel and Vyndamax.** There are no data available to support concomitant use.
- 3. Polyneuropathy of Hereditary Transthyretin–Mediated Amyloidosis (hATTR)** [Note: For patients with hATTR and cardiomyopathy or mixed phenotype {concurrent cardiomyopathy and polyneuropathy}, refer to FDA-Approved Indication, above]. Neither Vyndaqel nor Vyndamax are indicated for treatment of symptoms of polyneuropathy associated with hATTR.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

#### REFERENCES

1. Vyndaqel and Vyndamax [prescribing information]. New York, NY: Pfizer; May 2019.
2. Maurer MS, Schwartz JH, Gundapaneni B, et al. Tafamidis treatment for patients with transthyretin amyloid cardiomyopathy. *NEngl 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.