PRIOR AUTHORIZATION POLICY

POLICY: Amyloidosis – Tafamidis Products Prior Authorization Policy
- Vyndaqel (tafamidis meglumine capsules – Pfizer)
- Vyndamax (tafamidis capsules – Pfizer)

REVIEW DATE: 11/16/2022

OVERVIEW

Vyndaqel and Vyndamax are selective stabilizers of transthyretin (TTR) 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.[1] Studies excluded patients with New York Heart Association class IV disease.[2]

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.[2-8] 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 confirms the diagnosis of ATTR-CM.[8] 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.[7] Although many mutations have been identified, mutation of V122I is the most common in the US.[2-6] 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.[1]

Guidelines

The American Heart Association (AHA) scientific statement for the evolving diagnosis and management of cardiac amyloidosis (2020) recognizes tafamidis as a treatment for ATTR-CM.[7] They note that the benefit of tafamidis has not been observed in patients with NYHA class IV symptoms. Additionally, although combination use of tafamidis with Onpattro® (patisiran lipid complex intravenous infusion) or Tegsedi® (inotersen subcutaneous injection) is appealing to target both TTR silencing and stabilization for the remaining synthesized protein, this approach lacks data and may be cost-prohibitive. Tafamidis should generally be considered the agent of choice in ATTR-CM in patients with reasonable expected survival according to a position statement of the European Society of Cardiology (ESC) working group on myocardial and pericardial disease (2021).[8] The working group notes that tafamidis is the only drug that has shown efficacy in a randomized trial in patients with ATTR-CM and should be considered in patients with reasonable expected survival.

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 tafamidis products (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 tafamidis products (Vyndaqel and Vyndamax) is recommended in those who meet the following criteria:

FDA-Approved Indication

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 Amvuttra (vutrisiran subcutaneous injection), 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 Amvuttra, 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.[7] 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%). A scientific statement from the American Heart Association notes that there is little data to support combination therapy for these products.[8]

2. **Concurrent Use of Vyndaqel and Vyndamax.** There are no data available to support concomitant use.

3. **Polyneuropathy of Hereditary Transthyretin–Mediated Amyloidosis (hATTR).** Neither Vyndaqel nor Vyndamax are indicated for treatment of symptoms of polyneuropathy associated with hATTR.
   Note: For patients with hATTR and cardiomyopathy or mixed phenotype (concurrent cardiomyopathy and polyneuropathy), refer to FDA-Approved Indication, above.

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

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8. Kittleson MM, Maurer MS, Ambardekar AV, et al; on behalf of the American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology. AHA scientific statement: cardiac amyloidosis: evolving diagnosis and management. *Circulation.* 2020;142:e7-e22.
9. Garcia-Pavia P, Rapezzi C, Adler Y, et al. Diagnosis and treatment of cardiac amyloidosis: a position statement of the ESC working group on myocardial and pericardial disease. *Eur Heart J.* 2021;42:1554-1568.