



## PRIOR AUTHORIZATION POLICY

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

**REVIEW DATE:** 11/29/2023; selected revision 01/03/2024

### INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

## CIGNA NATIONAL FORMULARY COVERAGE:

### 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) to reduce cardiovascular mortality and cardiovascular-related hospitalization in adults.<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>2-8</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 confirms the diagnosis of ATTR-CM.<sup>8</sup> 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.<sup>7</sup> Although many mutations have been identified, mutation of V122I is the most common in the US.<sup>2-6</sup> 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 American Heart Association (AHA) scientific statement for the evolving diagnosis and management of cardiac amyloidosis (2020) recognizes tafamidis as a treatment for ATTR-CM.<sup>7</sup> 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).<sup>8</sup> 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. The American College of Cardiology (ACC) expert consensus decision pathway on comprehensive multidisciplinary care for patients with cardiac amyloidosis (2023) make similar comments and recommendations to the AHA and ESC regarding tafamidis.<sup>10</sup>

## **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.

- **Vyndaqel (tafamidis meglumine capsules – Pfizer)**
- **Vyndamax (tafamidis capsules – Pfizer)**

**is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):**

## **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  $\geq$  18 years of age; 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 COVERED**

- **Vyndaqel (tafamidis meglumine capsules – Pfizer)**
- **Vyndamax (tafamidis capsules – Pfizer)**

**is(are) considered experimental, investigational or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):**

**1. Concomitant Use With Amvuttra (vutrisiran subcutaneous injection), Onpattro (patisiran lipid complex intravenous infusion), Tegsedi (inotersen subcutaneous injection), or Wainua (eplontersen 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, Tegsedi, and Wainua did not allow concurrent use of tetramer stabilizers (e.g., tafamidis, diflunisal). The pivotal trials for Amvuttra and Wainua did not allow concurrent use of Onpattro or Tegsedi (Amvuttra was not approved when Eplontersen was under investigation). 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%). A scientific statement from the American Heart Association notes that there is little data to support combination therapy for these products.<sup>8</sup>

**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.

**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.
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10. Kittleson M, Ruberg FL, Ambardekar AV, et al. A report of the American College of Cardiology Solution Set Oversight Committee. 2023 ACC expert consensus decision pathway on comprehensive multidisciplinary care for the patient with cardiac amyloidosis. *JACC.* 2023;81(11):1076-1126.

**HISTORY**

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	11/16/2022
Annual Revision	No criteria changes.	11/29/2023
	<p>Conditions Not Covered</p> <p><b>Concomitant Use With Amvuttra (vutrisiran subcutaneous injection), Onpattro (patisiran lipid complex intravenous infusion), Tegsedi (inotersen subcutaneous injection), or Wainua (eplontersen subcutaneous injection).</b> Wainua was added to this condition not recommended for approval.</p>	01/03/2024

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