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Next Review Due By: 07/2024
Policy Number: C17345-A

Vyndaqel (tafamidis meglumine), Vyndamax (tafamidis)

PRODUCTS AFFECTED

Vyndaqel (tafamidis meglumine), Vyndamax (tafamidis)

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review.

A. CARDIOMYOPATHY:
1. Documented diagnosis of wild type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) AND
2. Documentation of BOTH of the following [DOCUMENTATION REQUIRED]:
   a. Member must have presence of amyloid deposits in biopsy tissue

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AND

b. Documentation of presence of a variant TTR genotype and/or TTR precursor protein identification by immunohistochemistry, scintigraphy, or mass spectrometry

AND

3. Documentation member has evidence of cardiac involvement by echocardiography with an end- diastolic interventricular septal wall thickness >12 mm
   AND
4. Documentation of the presence of clinical signs and symptoms of the disease (e.g., peripheral/autonomic neuropathy, motor disability, cardiovascular dysfunction, renal dysfunction) and baseline functional status assessment (e.g., 6 minute walk test [6MWT], Kansas City Cardiomyopathy Questionnaire-Overall Summary [KCCQ-OS]) to be used to assess drug therapy efficacy at renewal
   AND
5. Documentation of baseline clinical manifestations as evidenced by ONE of the following [DOCUMENTATION REQUIRED]:
   a. Documented diagnosis of NYHA functional class I, II or III heart failure with at least one prior hospitalization for heart failure
      OR
   b. Clinical evidence of HF (without hospitalization) manifested by signs or symptoms of volume overload or elevated intracardiac pressures (e.g. elevated jugular venous pressure, shortness of breath or signs of pulmonary congestion on x-ray or auscultation, peripheral edema) requiring treatment with a diuretic for improvement

   AND
6. Prescriber attests that member will not receive Vyndaqel or Vyndamax in combination with either of the following Oligonucleotide agents (e.g., patisiran, inotersen) AND Tetramer stabilizers (e.g., diflunisal)

CONTINUATION OF THERAPY:

A. CARDIOMYOPATHY:

1. Documentation of clinical improvement in symptoms or evidence of slowing of clinical decline OR decrease in number of hospitalizations since initial authorization, OR improvement or stabilization of the 6-minute walk test since initial authorization OR stable or improvement in KCCQ-OS [DOCUMENTATION REQUIRED]
   AND
2. Prescriber attests to or clinical review has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a cardiologist, geneticist, or a physician who specializes in the treatment of amyloidosis. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

18 years of age or older

QUANTITY:

Vyndaqel: 80 mg orally once daily (four 20 mg capsules)
Vyndamax: 61 mg orally once daily (one 61 mg capsule)
NOTE: Products are not substitutable

Maximum Quantity Limits –

HIGH RISK ALERT

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PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Transthyretin Stabilizer

FDA-APPROVED USES:
Indicated 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.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Transthyretin amyloidosis (ATTR) is an accumulation of transthyretin (TTR) amyloid fibrils in various tissues. TTR is a 127 amino acid protein that forms a tetrameric transport protein primarily synthesized in the liver. The hereditary form of ATTR is caused by autosomal dominant mutations in the TTR gene. These mutations lead to abnormally folded monomers that self-assemble to create amyloid fibrils; they are then deposited extracellularly in various tissues. There are more than 120 reported TTR single point mutations, with the most common mutations being T60A, V30M, and V122I. These mutations can lead to polyneuropathy, autonomic neuropathy, cardiomyopathy, ocular manifestations, or a mixture of those listed.

Symptoms associated with polyneuropathy include paresthesia, hypesthesia, carpal tunnel syndrome, and motor neuropathy. Symptoms of autonomic neuropathy include orthostatic hypotension, constipation alternating with diarrhea, nausea, vomiting, delayed gastric emptying, erectile dysfunction, anhidrosis, urinary retention, and incontinence. Symptoms of cardiomyopathy include myocardial stiffness, reduction in chamber capacity, and congestive heart failure. Early- onset ATTR-FAP develops between the late 20s to the early 40sand is characterized by a predominant loss of superficial sensation, presence of family history, high penetrance rate, severe autonomic dysfunction, and atrioventricular conduction block requiring pacemaker implantation. On the other hand, late-onset ATTR-FAP develops after 50 years of age and is characterized by sensorimotor symptoms beginning in the distal lower extremities, initial involvement of both superficial and deep sensations, loss of all sensory modalities except sensory dissociation, low penetrance rate, relatively mild autonomic dysfunction, frequent presence of cardiomegaly, and extreme male preponderance.

Risk factors for TTR-FAP differ among members with their specific mutations. Members with Val30Met mutations are likely to present polyneuropathy and may present cardiomyopathy characterized by arrhythmias

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and heart failure near the end of the member's lifespan. The Val122Ile mutation is associated with cardiomyopathy with symptoms of heart failure, such as edema and shortness of breath.

Diagnosis requires both member history and confirmation.
Member history and physical examination includes family history of genetic disease and multisystem red-flag signs and/or symptoms. Confirmation using accurate diagnostic tools includes histopathology and genetic testing (TTR genotyping). Examples of histopathology are tissue biopsy of labial salivary gland, abdominal subcutaneous adipose tissue, gastrointestinal tract, and nerve tissue using Congo red stain or TTR immunolabeling, and immunohistochemistry. Examples of genetic testing include a targeted approach to detect pathogenic mutation in members with a positive family history. TTR gene sequencing may be required to detect suspected and new pathogenic mutations in members without positive family history or with atypical symptoms. Members with stage 0 FAP are asymptomatic, members with stage I FAP are ambulatory, members with stage II FAP require assistance but are ambulatory, and members with stage III are wheelchair bound or bedridden.
Prognosis for members who are untreated have approximately three to fifteen years to live due to progressive symptoms, heart failure, and sudden death.
The only current treatment for stage 0 and stage 1 TTR-FAP is orthotopic liver transplant. Liver transplants in members with stage 2 or 3 TTR-FAP are not recommended due to complications that may arise from the neuropathy or amyloid cardiomyopathy. Patisiran has just been approved in the U.S. for the treatment of polyneuropathy of hATTR, and tafamidis is approved for stage 1 TTR-FAP by the European Medicines Agency. Other pharmacotherapies that are currently in clinical trials for the treatment of ATTR amyloidosis include:

- Diflunisal, a non-steroidal anti-inflammatory drug that prevents disaggregation and amyloid fibril formation as well as stabilizes TTR
- ISIS-TTRRx, an antisense therapy that reduces TTR mRNA expression
- Doxycycline/tauroursodeoxycholic acid, a combination of an antibiotic which reduces the formation of amyloid fibrils and a drug that reduces TTR deposition There is no data to support using pharmacotherapy for stage 0 and stage 3 TTR- FAP. Only members with stage 1 or 2 disease should receive disease-modifying pharmacotherapy

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Vyndaqel (tafamidis meglumine), Vyndamax (tafamidis) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. There are no labeled contraindications to Vyndaqel (tafamidis meglumine), Vyndamax (tafamidis).

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Vyndaqel CAPS 20MG (bottle of 120)
Vyndamax CAPS 61MG (bottle of 30)

REFERENCES

1. Vyndaqel (tafamidis meglumine) and Vyndamax (tafamidis) [prescribing information]. New York,

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NY: Pfizer Labs; April 2023.
2. Maurer MS, Schwartz JH, Gundepaneni B, et al. Tafamidis Treatment for Members with Transthyretin Amyloid Cardiomyopathy. N Engl J Med 2018; 379:1007-1016. Sept 13,2018
3. Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013;8(1):1-18. doi:10.1186/1750- 1172-8-31
4. Maurer M, Schwartz JH, Gundapaneni B, et al. Tafamidis treatment for members with transthyretin amyloid cardiomyopathy. N Engl J Med. 2018;379:1007-16. doi: 10.1056/NEJMoa1805689.27 NCT01994889
5. Gertz MA, Benson MD, Dyck PJ, et al. Diagnosis, prognosis, and therapy of transthyretin amyloidosis. J Am Coll Cardiol. 2015;66(21):2451-2466. doi:10.1016/j.jacc.2015.09.075
6. Kittleson, M. M., Maurer, M. S., Ambardekar, A. V., Bullock-Palmer, R. P., Chang, P. P., Eisen, H. J., … Ruberg, F. L. (2020). Cardiac amyloidosis: Evolving diagnosis and management: A scientific statement from the American Heart Association. Circulation, 142(1). doi:10.1161/cir.0000000000000792

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Prescriber Requirements References	Q3 2023
REVISION- Notable revisions: Required Medical Information Continuation of Therapy References	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file

HIGH RISK ALERT

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