SmartPA Criteria Proposal

Drug/Drug Class:	Transthyretin-Mediated Amyloidosis (ATTR) Clinical Edit
First Implementation Date:	May 16, 2019
Proposed Date:	October 17, 2023
Prepared for:	MO HealthNet
Prepared by:	MO HealthNet/Conduent
Criteria Status:	☒Existing Criteria ☐Revision of Existing Criteria ☐New Criteria

Executive Summary

Purpose: Ensure appropriate utilization and control of agents for transthyretin-mediated amyloidosis (ATTR)

Why Issue Selected: Transthyretin-mediated amyloidosis (ATTR) is a form of systemic amyloidosis caused by amyloid deposits made up of a protein called transthyretin (TTR). ATTR can be either hereditary or acquired (non-hereditary). TTR is always present in the blood, where it transports thyroid hormone (thyroxine) and vitamin A (retinol), hence the name: "trans-thy-retin". When the abnormal proteins are produced and the fibers attach and deposit in organs and other places in the body, normal function of that part of the body is affected. The hereditary form of ATTR is caused by a pathogenic variant in the TTR gene that causes misfolding of the tetramer subunits, while the wild-type form is associated with misfolding of destabilized native protein (particularly in the elderly) and causes non-familial cases. ATTR is a rare disease, affecting less than 200,000 people in the US.

Onpattro® (patisiran), Tegsedi® (inotersen), and Amvuttra™ (vutrisiran) are indicated for the treatment of the polyneuropathy caused by hereditary transthyretin-mediated amyloidosis (hATTR-PN) in adults. These agents work by targeting RNA to reduce the production of the TTR protein thus reducing the accumulation of amyloid deposits in the peripheral nerves, improving symptoms, and helping patients better manage the condition. hATTR-PN affects approximately 3,000 people in the United States. The use of Tegsedi requires prescribers and patients to enroll in a Risk Evaluation and Mitigation Strategies (REMS) program due to its potential to cause thrombocytopenia and glomerulonephritis that may require immunosuppressive treatment and may result in dialysis.

Vyndaqel® (tafamidis meglumine) and Vyndamax® (tafamidis) are indicated for the treatment of cardiomyopathy caused by transthyretin-mediated amyloidosis (ATTR-CM) in adults. These agents are for both wild-type transthyretin amyloidosis (ATTRwt) and hereditary transthyretin amyloidosis (hATTR). ATTR-CM results in accumulation of amyloid fibrils in the left ventricle which ultimately causes the myocardium to become stiff, resulting in heart failure. It is estimated that 100,000 people in the US are affected by ATTR-CM. Vyndaqel and Vyndamax are oral TTR stabilizers that selectively bind to TTR, stabilizing the tetramer of the TTR transport protein and slowing the formation of amyloid that causes ATTR-CM.

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Due to the high cost, possible adverse events, and specific approved indications, MO HealthNet will impose clinical criteria to ensure appropriate utilization of agents for ATTR.

Program-Specific Information:

Date Range FFS 07/01/2022 to 06/30/2023			
Drug	**Claims**	**Spend**	**Average Spend per Claim**
AMVUTTRA 25MG/0.5ML SYR	0	-	-
ONPATTRO 10MG/5ML VIAL	0	-	-
TEGSEDI 284MG/1.5ML SYR	0	-	-
VYNDAQEL 20MG CAPSULE	3	$61,513.90	$20,504.63
VYNDAMAX 61MG CAPSULE	10	$85,937.24	$8,593.72

Type of Criteria:
☒ **Increased risk of ADE**
☒ **Appropriate Indications**
☐ **Preferred Drug List**
☒ **Clinical Edit**

Data Sources:
☐ **Only Administrative Databases**
☒ **Databases + Prescriber-Supplied**

Setting & Population

- Drug class for review: Agents for transthyretin-mediated amyloidosis (ATTR)
- Age range: All appropriate MO HealthNet participants aged 18 years and older

Approval Criteria

- Participant is aged 18 years or older **AND**
- For documented diagnosis of polyneuropathy caused by hATTR:
  - Onpattro, Tegsedi, and Amvuttra only **AND**
  - Documented transthyretin variant by genotyping **AND**
  - Documented amyloid deposit by tissue biopsy or scintigraphy scan (e.g., Tc-99m PYP scan) **AND**
  - First claim prescribed by a neurologist or other appropriate specialist in the treated disease state **AND**
  - For Tegsedi:
    - Documentation of laboratory tests prior to treatment, including platelet count, serum creatinine, estimated glomerular filtration rate (eGFR), urine protein to creatinine ratio (UPCR), and urinalysis
    - Limit of 1 syringe (1.5ml) every 7 days
    - Initial approval duration of 6 months in order to reevaluate therapy and ensure proper monitoring has occurred with regards to platelet count, serum creatinine, eGFR, UPCR, and urinalysis as needed. If criteria are met to continue therapy, 6-month renewal PA can be given with re-review required again in 6 months.
- For documented diagnosis of cardiomyopathy caused by ATTR:
  - Vyndaqel or Vyndamax only **AND**
  - First claim prescribed by a cardiologist or other appropriate specialist in the treated disease state **AND**
  - Documented amyloid deposition by tissue biopsy or scintigraphy scan (e.g., Tc-99m PYP scan) **AND**
  - NYHA functional Class I-III **AND**
  - Documented diagnosis of heart failure **AND**
  - Documented echocardiogram with end-diastolic interventricular septal wall thickness > 12 mm **AND**
  - Limit of 120 capsules every 30 days for Vyndaqel **OR**
  - Limit of 30 capsules every 30 days for Vyndamax

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- Initial approval duration of 6 months to reevaluate therapy and assessment of efficacy (slowing of clinical decline, decrease in cardiovascular related hospitalizations, improvement in 6-minute walk test, and/or stable or improvement in the Kansas City Cardiomyopathy Questionnaire-Overall Summary (KCCQ-OS)). If criteria are met to continue therapy, 6 month renewal PA can be given with re-review required again in 6 months.

Denial Criteria

- Therapy will be denied if all approval criteria are not met
- For Onpattro, Tegsedi, and Amvuttra: concurrent therapy with Vyndaqel or Vyndamax
- For Vyndaqel or Vyndamax:
  - concurrent therapy with Onpattro, Tegsedi, or Amvuttra **OR**
  - NYHA finctional Class IV **OR**
  - presence of a cardiac mechanical assist device

Required Documentation

Laboratory Results:	X	Progress Notes:	X
MedWatch Form:		Other:	X

Disposition of Edit

Denial: Exception “0682” (Clinical Edit)
Rule Type: CE

Default Approval Period

6 months

References

- Onpattro (patisiran) [prescribing information]. Cambridge, MA: Alnylam Pharmaceuticals, Inc; January 2023.
- Tegsedi (inotersen) [prescribing information]. Carlsbad, CA: Ionis Pharmaceuticals, Inc; June 2022.
- Vyndaqel/Vyndamax (tafamidis) [package insert]. New York, NY: Pfizer Labs; June 2021.
- Amvuttra (vutrisiran) [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; February 2023.
- Amyloidosis Foundation. Amyloidosis Facts. https://amyloidosis.org/facts/. Accessed August 23, 2023.
- Roberts, J, Besa, E. Transthyretin-Related Amyloidosis. Medscape. Transthyretin-Related Amyloidosis: Practice Essentials, Background, Pathophysiology (medscape.com). Updated July 19, 2022. Accessed August 23, 2023.
- IPD Analytics. New Drug Approval: Onpattro (patisiran). August 2018.
- IPD Analytics. New Drug Approval: Tegsedi (inotersen). October 2018.
- IPD Analytics. New Drug Approval: Vyndamax and Vyndaqel. May 2019.
- IPD Analytics. New Drug Review: Amvuttra (vutrisiran). July 2022.

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