Addendum to the Protocol for Transthyretin-Mediated Amyloidosis (ATTR) Products
July 2025

DURB Approval Date	**10/2019, 10/2024, 7/2025**
Commissioners Approval Date	**1/2025**

Non-Preferred Agents:
Onpattro (patisiran)
Vyndaqel and Vyndamax (tafamidis meglumine)
Tegsedi (inotersen)
Amvuttra (vutrisiran)
Wainua (eplontersen)
Attruby (acoramidis)

Addendum:

The purpose of this addendum is to add Attruby, a new drug approved by the FDA in November 2024. In addition, the protocol has been updated to include a new indication approved by the FDA on March 2025 for Amvuttra.

Background:

Onpattro (patisiran) and Amvuttra (vutrisiran) contain a transthyretin-directed small interfering RNA and are indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults. Amvuttra is also FDA approved for the treatment of cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis in adults to reduce cardiovascular mortality, cardiovascular hospitalizations and urgent heart failure visits.

Vyndaqel (tafamidis meglumine), **Vyndamax** (tafamidis), and Attruby (acoramidis) are transthyretin stabilizers indicated for the treatment of the cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis in adults to reduce cardiovascular mortality and cardiovascular-related hospitalization.

Tegsedi (inotersen) and **Wainua (eplontersen)** are a transthyretin-directed antisense oligonucleotide indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

Criteria for approval:

1. Documentation of diagnosis is confirmed by genotyping, biopsy, immunohistochemical analysis, scintigraphy, or mass spectrometry

2. Medication is prescribed by or in consultation with a neurologist, cardiologist, or other specialist(s) with expertise in the treatment of ATTR

3. Patient has clinical signs and symptoms of ATTR (e.g., peripheral sensorimotor polyneuropathy, motor disability, cardiovascular dysfunction, or carpal tunnel syndrome)

4. Patient's weight should be made available for drugs that have weight-based dosing. Patient's height and weight should be made available for drugs that have dosing based on body surface area

5. Patient is of the FDA-labeled or compendial approved age

6. Patient has no FDA-labeled contraindications to the requested drug

7. The medication requested is prescribed in accordance with a Food and Drug Administration (FDA)-established indication and dosing regimens or in accordance with a medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer-reviewed evidence

8. Medication will not be used concurrently with other transthyretin-mediated amyloidosis (ATTR) products

9. For Onpattro, Amvuttra, Tegsedi and Wainua: patient has a diagnosis of the polyneuropathy of hereditary transthyretin-mediated amyloidosis

10. For Vyndaqel and Vyndamax, Amvuttra, and Attruby: patient is using medication to treat cardiomyopathy of wild type or hereditary/variant transthyretin-mediated amyloidosis (ATTR-CM) to reduce any one of the following:
    a. Cardiovascular mortality (Amvuttra, Attruby, Vyndaqel and Vyndamax)
    b. Cardiovascular-related hospitalization (Amvuttra, Attruby, Vyndaqel and Vyndamax)
    c. Urgent heart failure visits (Amvuttra)

Continuation of therapy:

1. Documentation that patient has experienced a positive clinical response to medication (e.g., improved neurologic impairment, motor function, quality of life)

2. Medication is not used concurrently with other transthyretin-mediated amyloidosis (ATTR) products

3. The medication requested is prescribed in accordance with a Food and Drug Administration (FDA)-established indication and dosing regimens or in accordance with a medically-appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer-reviewed evidence

4. For dose increases, patient's weight should be made available for drugs that have weight-based dosing. Patient's height and weight should be made available for drug that have dosing based on body surface area

NOTE: There is a BOXED WARNING OF THROMBOCYTOPENIA AND GLOMERULONEPHRITIS for Tegsedi. Tegsedi is available only through a restricted distribution program called the Tegsedi REMS Program.

Initial and Renewal Approval Duration: 12 Months

Quantity Level Limit: Reference formulary for drug specific quantity level limits

References:

1. Onpattro® [package insert]. Alnylam Pharmaceuticals, Inc. San Diego, CA 92121. January 2023.
2. Vyndaqel® (tafamidis meglumine) and Vyndamax® (tafamidis) [package insert]. Pfizer Labs Inc. NY,

NY 10017. May 2019.
3. Tegsedi® [package insert]. Ionis Pharmaceuticals, Inc. Carlsbad, CA 92010. January 2024.
4. Amvuttra® [package insert]. Alnylam Pharmaceuticals, Inc., Cambridge, MA 02142. March 2025.
5. Wainua® (eplontersen) [package insert] AstraZeneca Pharmaceuticals LP, Wilmington, DE 19850. April 2025.
6. Attruby® (acoramidis) [package insert]. BridgeBio Pharma, Inc. Palo Alto, CA 94304. November 2024
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15. Benson MD, Waddington-Cruz M, Berk JL. Inotersen Treatment for Patients with Hereditary Transthyretin Amyloidosis. N Engl J Med 2018;379:22 -31
16. Ando Y, Waddington-Cruz M, Sekijima Y, Koike H, Ueda M, Konishi H, Ishii T, Coelho T. Optimal practices for the management of hereditary transthyretin amyloidosis: real-world experience from Japan, Brazil, and Portugal. Orphanet J Rare Dis. 2023 Oct 12;18(1):323. doi: 10.1186/s13023-023-02910-3. PMID: 37828588; PMCID: PMC10571420.
17. Poli L, Labella B, Cotti Piccinelli S, Caria F, Risi B, Damioli S, Padovani A and Filosto M (2023) Hereditary transthyretin amyloidosis: a comprehensive review with a focus on peripheral neuropathy. *Front.Neurol.* 14:1242815. doi: 10.3389/fneur.2023.1242815.