Tafamidis Meglumine (Vyndaqel) and Patisiran (Onpattro)
Treatment of polyneuropathy associated with amyloidosis
Criteria for Use
September 2019
VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.
See the VA National PBM-MAP-VPE Monograph on this drug at the PBM INTERNet or PBM INTRANet site for further information.

Inclusion Criteria
The answers to all the following must be fulfilled to receive patisiran or tafamidis meglumine.

☐ Tafamidis meglumine is the preferred therapy in patients initiating therapy. Patients may only receive patisiran if a patient has a;
   ○ Documented allergy to tafamidis meglumine
   OR
   ○ Lack of clinical response to an appropriate trial of tafamidis meglumine (treatment for 9 months)

☐ Patients should have a baseline Neuropathy Impairment score–Lower Limb (NIS LL), Polyneuropathy Disability Score (PND) or Familial Amyloid Polyneuropathy (FAP) in their medical record so they can be monitored for success of therapy. Only one of the suggested scales need be used.

☐ Prescribing of these agents is restricted to neurology or locally designated hATTR provider

☐ The patient has a diagnosis of hereditary transthyretin amyloidosis (hATTR) polyneuropathy based on:
   ○ Clinical signs and symptoms,
   and
   ○ Genetic testing that confirms a pathogenic variant in TTR
   ○ The patient has peripheral neuropathy associated with hATTR with:
      ▪ A baseline Neuropathy Impairment score–Lower Limb (NIS LL)
      ▪ A baseline polyneuropathy disability (PND) score of IIIb or lower
      ▪ A baseline Familial Amyloid Polyneuropathy (FAP) stage of 1 or 2
   and

☐ Age 18-85 years
☐ Anticipated Survival > 2 years

☐ Supplementation at the recommended daily allowance of vitamin A is advised for patients taking patisiran. Patients should be referred to eye clinic if they develop ocular symptoms suggestive of vitamin A deficiency (e.g., night blindness). (Applies only to patisiran).

For women of childbearing potential:

☐ Pregnancy should be excluded prior to receiving patisiran or tafamidis meglumine and the patient provided contraceptive counseling on potential risks vs. benefits of taking these agents.
For continuation of therapy

Documentation of response at 9 months (BOTH are required to continue therapy):
- The patient continues to have a PND score of IIIb or lower or FAP stage 1 or 2, AND
- The patient has documentation of positive clinical response (e.g. improved motor function, quality of life, or ambulation or decreased neurological impairment).

Exclusion Criteria
If the answer to ANY item below is met, then the patient should NOT receive patisiran or tafamidis meglumine.
- Sensorimotor or autonomic neuropathy not related to hATTR including neuropathy due to uncontrolled diabetes
- Primary amyloidosis
- Leptomeningeal amyloidosis
- Patient currently receiving therapy with diflunisal or doxycycline
- Severe reaction to a liposomal product or hypersensitivity to oligonucleotides (patisiran)
- Prior liver transplant

Polyneuropathy Disability Score (PND)
Stage 0: no impairment
Stage I: sensory disturbances but preserved walking capability
Stage II: impaired walking capability but ability to walk without a stick or crutches
Stage IIIa: walking only with the help of one stick or crutch
Stage IIIb: walking with the help of two sticks or crutches
Stage IV: confined to a wheelchair or bedridden

Familial Amyloid Polyneuropathy (FAP) Score
Stage 1
Symptoms are mild at this stage, with the functioning of the lower limbs affected but not impaired. This is the stage for early detection of FAP symptoms.

Stage 2
Symptoms turn from mild to moderate in severity in stage 2. Lower limb function is even more affected, with patients possibly requiring walking assistance. Further damage to nerves caused by amyloid deposits is observed.

Stage 3
Symptoms have significantly worsened in stage 3, and the patient needs a wheelchair for mobility. There is no data to support the efficacy of drug therapies at this stage of the disease.
**Neuropathy Impairment score—Lower Limb (NIS LL)**

**Table 1.** Scoring used by the NIS-LL to grade motor activity (muscle power) in the lower limbs of patients with neurological deficits [14–16]

<table>
<thead>
<tr>
<th>NIS-LL score</th>
<th>Muscle power grading</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>normal</td>
</tr>
<tr>
<td>1</td>
<td>25% weak</td>
</tr>
<tr>
<td>2</td>
<td>50% weak</td>
</tr>
<tr>
<td>3</td>
<td>75% weak</td>
</tr>
<tr>
<td>3.25</td>
<td>movement against gravity</td>
</tr>
<tr>
<td>3.50</td>
<td>movement with gravity eliminated</td>
</tr>
<tr>
<td>3.75</td>
<td>muscle flicker, no movement</td>
</tr>
<tr>
<td>4</td>
<td>paralysis</td>
</tr>
</tbody>
</table>

**Table 2.** Muscle groups evaluated by the NIS-LL to assess motor activity in the lower limbs of patients with neurological deficits

<table>
<thead>
<tr>
<th>Muscle groups tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip flexion</td>
</tr>
<tr>
<td>Hip extension</td>
</tr>
<tr>
<td>Knee flexion</td>
</tr>
<tr>
<td>Knee extension</td>
</tr>
<tr>
<td>Ankle dorsiflexion</td>
</tr>
<tr>
<td>Ankle plantar flexion</td>
</tr>
<tr>
<td>Toe extension</td>
</tr>
<tr>
<td>Toe flexion</td>
</tr>
</tbody>
</table>

**Scoring methodology**

0-4 points per side per muscle group; total of 64 points if paraplegic

The power of each muscle group is evaluated bilaterally [14–16].

**Table 3.** Scoring used by the NIS-LL to grade sensory and reflex activity in the lower limbs of patients with neurological deficits

<table>
<thead>
<tr>
<th>NIS-LL score</th>
<th>Sensory/reflex activity grading</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>normal</td>
</tr>
<tr>
<td>1</td>
<td>decreased</td>
</tr>
<tr>
<td>2</td>
<td>absent</td>
</tr>
</tbody>
</table>

Sensory stimuli are applied to each side of the dorsal surface of the great toe at the terminal phalanx [14–16].

**Table 4.** Modalities and reflexes tested by the NIS-LL

<table>
<thead>
<tr>
<th>Reflexes tested</th>
<th>Modality tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quadriceps</td>
<td>Touch pressure</td>
</tr>
<tr>
<td>Ankle</td>
<td>Pinprick</td>
</tr>
<tr>
<td></td>
<td>Vibration (165 Hz) tuning fork</td>
</tr>
</tbody>
</table>

**Scoring methodology**

0–2 points per side per reflex; total of 8 possible points if areflexic

Age-adjusted scoring; decreased ankle reflexes are considered normal for patients aged 50–69 years and scored as 0 and absent reflexes for patients >70 years are considered normal and scored as 0

0–2 points per side per modality; total of 16 points if lacking all sensation at the great toe

For reflexes, stimuli are applied to the quadriceps and ankle tendons bilaterally [14–16].

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