Hereditary ATTR amyloidosis: a life-threatening, multisystem disease\textsuperscript{1-4}

Hereditary ATTR (hATTR) amyloidosis is an inherited, rapidly progressive, life-threatening disease.\textsuperscript{2,3,5} It is caused by a mutation in the transthyretin (TTR) gene that results in misfolded TTR proteins accumulating as amyloid fibrils in multiple sites including the nerves, heart, and gastrointestinal tract.\textsuperscript{2,6,7} Patients with hATTR amyloidosis can present with symptoms across a spectrum that includes\textsuperscript{1,3,4}:

- Peripheral sensory-motor neuropathy
- Autonomic dysfunction
- Cardiomyopathy

**Constellation of possible signs and symptoms of hATTR amyloidosis**

- **CNS manifestations**
  - Progressive dementia
  - Headache
  - Ataxia
  - Seizures
  - Spastic paresis
  - Stroke-like episodes

- **Ocular manifestations**
  - Vitreous opacification
  - Glaucoma
  - Abnormal conjunctival vessels
  - Papillary abnormalities

- **Cardiovascular manifestations**
  - Conduction block
  - Cardiomyopathy
  - Arrhythmia

- **Autonomic neuropathy**
  - Orthostatic hypotension
  - Recurrent urinary tract infections (due to urinary retention)
  - Sexual dysfunction
  - Sweating abnormalities

- **Nephropathy**
  - Proteinuria
  - Renal failure

- **Gl manifestations**
  - Nausea & vomiting
  - Early satiety
  - Diarrhea
  - Severe constipation
  - Alternating episodes of diarrhea & constipation
  - Unintentional weight loss

- **Peripheral sensory-motor neuropathy**
  - Neuropathic pain
  - Altered sensation (ie, change in sensitivity to pain and temperature)
  - Numbness and tingling
  - Muscle weakness
  - Impaired balance
  - Difficulty walking

- **Carpal tunnel syndrome**

Symptom presentation can be highly varied even among individuals in the same family. However, certain symptom clusters should raise suspicion of a single underlying condition.\textsuperscript{1,8}


See the reverse side to learn how to recognize the red-flag symptoms of hATTR amyloidosis.
Recognize the red flags.
Suspect hereditary ATTR amyloidosis.

Patients with hATTR amyloidosis require an early and accurate diagnosis due to the rapid natural progression of the disease\(^1,9,10\)

The clinical manifestation of hATTR amyloidosis can vary widely, and recognizing the signs can be crucial to an early diagnosis.\(^1\)

The combination of peripheral neuropathy with autonomic dysfunction or cardiac involvement may indicate hATTR amyloidosis\(^1\)

### Progressive symmetric sensory-motor neuropathy and ≥1 of the following:

- **Bilateral carpal tunnel syndrome**
- **Nephropathy** (e.g., proteinuria or renal failure)
- **Early autonomic dysfunction** (e.g., erectile dysfunction or postural hypotension)
- **Gastrointestinal complaints** (e.g., chronic diarrhea, constipation, or diarrhea/constipation)
- **Unexplained weight loss**
- **Cardiovascular manifestations** (e.g., conduction block, cardiomyopathy, or arrhythmia)
- **Vitreous opacities**
- **Positive family history**

**Additional signs: Rapid disease progression or failure to respond to immunomodulatory treatment**


To learn more about hATTR amyloidosis and genetic screening made available at no charge through Alnylam Act™, visit [www.hattramyloidosis.com](http://www.hattramyloidosis.com).