

# ONPATTRO™ (patisiran) Product Fact Sheet

- ONPATTRO™ (patisiran) lipid complex injection is approved by the United States Food and Drug Administration (FDA) for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults.
- hATTR amyloidosis is a rapidly progressive and life-threatening disease.<sup>1,2,3</sup>
- The condition is caused by a mutation in the transthyretin (TTR) gene that results in the accumulation of amyloid deposits in multiple organs of the body, including the nerves, heart, and gastrointestinal (GI) tract.<sup>1,2,3</sup>
- ONPATTRO is an RNAi therapeutic designed to silence messenger RNA, thereby inhibiting synthesis of TTR protein and preventing further deposition of the TTR amyloid in tissues.<sup>4</sup>
- ONPATTRO is the first FDA-approved RNA interference (RNAi) therapeutic, a new class of medicines that harness the natural biological process of RNAi.
- In the largest controlled study of hATTR amyloidosis, ONPATTRO was shown to improve polyneuropathy, as measured by the modified Neuropathy Impairment Score (mNIS+7) – with reversal of neuropathy impairment in a majority of patients – and to improve quality of life, reduce autonomic symptoms, and improve activities of daily living.<sup>5</sup>
- ONPATTRO is administered via intravenous (IV) infusion once every three weeks and the dose is based on actual body weight. Home infusion may be an option for some patients after an evaluation and recommendation by the treating physician, and may not be covered by all insurance plans. Regardless of the setting, ONPATTRO infusions should be performed by a healthcare professional. For more information about ONPATTRO, please visit ONPATTRO.com.

## ONPATTRO Research at a Glance

- The FDA approval of ONPATTRO was based on positive results from the randomized, double-blind, placebo-controlled, global Phase 3 APOLLO study, the largest-ever study in hATTR amyloidosis patients with polyneuropathy.<sup>5</sup>
- The primary endpoint of the APOLLO study was the change from baseline in the modified Neuropathy Impairment Score +7 (mNIS+7), which assesses motor strength, reflexes, sensation, nerve conduction and postural blood pressure.<sup>5</sup>
  - » Patients treated with ONPATTRO had a mean 6.0-point decrease (improvement) in mNIS+7 score from baseline compared to a 28.0-point mean increase (worsening) for patients in the placebo group, resulting in a 34.0-point mean difference relative to placebo, after 18 months of treatment.<sup>5</sup>
  - » While nearly all ONPATTRO-treated patients experienced a treatment benefit relative to placebo, 56 percent of ONPATTRO-treated patients at 18 months of treatment experienced reversal of neuropathy impairment (a decrease from baseline in mNIS+7), compared to four percent of patients who received placebo.<sup>5</sup>
  - » Over 18 months of treatment, patients treated with ONPATTRO experienced significant benefit vs. placebo for all other secondary efficacy endpoints including measures of activities of daily living, walking ability, nutritional status, and autonomic symptoms.<sup>5</sup>
  - » As measured by the Norfolk Quality of Life Diabetic Neuropathy (QoL-DN) Score, 51 percent of patients treated with ONPATTRO experienced improvement in quality of life at 18 months relative to their own baseline, compared to 10 percent of the placebo-treated patients.<sup>5</sup>
  - » The most common adverse events that occurred more frequently with ONPATTRO than with placebo were upper respiratory tract infections and infusion-related reactions. To reduce the risk of infusion-related reactions, patients received premedications prior to infusion.<sup>5</sup>

**Please see Important Safety Information on the next page.**

**onpattro**  
(patisiran) lipid complex  
injection 



## RNAi, A Major New Class of Medicines

- Historically, RNA was only thought to be involved in protein synthesis. However, in recent years, RNAs have been identified to also play significant roles in regulatory functions within the cell.<sup>6</sup>
- A specific class of RNA, called small-interfering RNA (siRNA), appeared to exert cellular control resulting in gene silencing.<sup>7</sup> In 2001, researchers confirmed that siRNA-mediated gene silencing did occur in human cells.<sup>8</sup> This form of gene silencing has since become widely known as RNA interference, or RNAi for short.
- The FDA approval of ONPATTRO marks the arrival of RNAi therapeutics, an entirely new class of medicines to address the needs of patients with limited treatment options.
- ONPATTRO is the result of countless contributors who have overcome enormous scientific and business challenges to make RNAi therapeutics a reality.

## Access to ONPATTRO: Alnylam Assist™

As part of Alnylam's commitment to making therapies available to those who will benefit from them, Alnylam Assist will offer a wide range of services to guide patients through treatment with ONPATTRO, including, explaining insurance coverage, financial assistance programs for eligible patients, educational materials to help facilitate conversations with doctors and family, and assistance with connecting to local resources. Patients will have access to dedicated Case Managers and Patient Education Liaisons throughout their treatment with ONPATTRO. The goal of Alnylam Assist is to provide comprehensive support and guidance to patients prescribed ONPATTRO. Visit [AlnylamAssist.com](http://AlnylamAssist.com) for more information.

<sup>1</sup> Adams D, Coelho T, Obici L, et al, *Neurology*. 2015;85(8):675-682.

<sup>2</sup> Conceicao, et al, *Journal of the Peripheral Nervous System*. 2016;21:5-9.

<sup>3</sup> Shin, et al, *Mt Sinai J Med*. 2012;79(6):733-748.

<sup>4</sup> ONPATTRO [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc; 2018.

<sup>5</sup> Adams D, et al, *N Engl J Med*. 2018;378(27).

<sup>6</sup> Couzin J. *Science*. 2002;298:2296-7.

<sup>7</sup> Fire A, Xu S, Montgomery MK, et al, *Nature*. 1998;391:806-11.

<sup>8</sup> Elbashir SM, Harborth J, Lendeckel W. *Nature*. 2001;411:494-8.

## IMPORTANT SAFETY INFORMATION

### Infusion-Related Reactions

Infusion-related reactions (IRRs) have been observed in patients treated with ONPATTRO. In a controlled clinical study, 19% of ONPATTRO-treated patients experienced IRRs, compared to 9% of placebo-treated patients. The most common symptoms of IRRs with ONPATTRO were flushing, back pain, nausea, abdominal pain, dyspnea, and headache.

To reduce the risk of IRRs, patients should receive premedication with a corticosteroid, acetaminophen, and antihistamines (H1 and H2 blockers) at least 60 minutes prior to ONPATTRO infusion. Monitor patients during the infusion for signs and symptoms of IRRs. If an IRR occurs, consider slowing or interrupting the infusion and instituting medical management as clinically indicated. If the infusion is interrupted, consider resuming at a slower infusion rate only if symptoms have resolved. In the case of a serious or life-threatening IRR, the infusion should be discontinued and not resumed.

### Reduced Serum Vitamin A Levels and Recommended Supplementation

ONPATTRO treatment leads to a decrease in serum vitamin A levels. Supplementation at the recommended daily allowance (RDA) of vitamin A is advised for patients taking ONPATTRO. Higher doses than the RDA should not be given to try to achieve normal serum vitamin A levels during treatment with ONPATTRO, as serum levels do not reflect the total vitamin A in the body.

Patients should be referred to an ophthalmologist if they develop ocular symptoms suggestive of vitamin A deficiency (e.g. night blindness).

### Adverse Reactions

The most common adverse reactions that occurred in patients treated with ONPATTRO were upper respiratory tract infections (29%) and infusion related reactions (19%).

For additional information about ONPATTRO, please see the full [Prescribing Information](#).

