Onpattro™ (patisiran) – New orphan drug approval

- On August 10, 2018, Alnylam announced the FDA approval of Onpattro (patisiran), for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults.
    - Onpattro is the first and only FDA-approved treatment available for this indication in the U.S.
- Affecting about 50,000 people worldwide, hATTR amyloidosis is a rare, progressively debilitating and often fatal genetic disease characterized by the buildup of abnormal amyloid protein in body organs and tissue, such as the peripheral nerves and heart. This results in peripheral neuropathy, autonomic neuropathy, and cardiomyopathy, as well as other disease manifestations. The median survival is 4.7 years following diagnosis.
- Onpattro is the first approved agent in a new class of drugs called small interfering ribonucleic acid (siRNA) treatment, which interfere with the portion of the RNA involved in causing the disease. Specifically, hATTR amyloidosis is caused by mutations in the transthyretin (TTR) gene. Onpattro encases the siRNA into a lipid nanoparticle to deliver the drug directly into the liver, where the TTR protein is primarily produced, in order to alter or halt the production of this disease-causing protein.
- The safety and efficacy of Onpattro was based on the APOLLO study involving 225 hATTR amyloidosis patients. Patients were randomized to receive Onpattro or placebo once every 3 weeks for 18 months. The primary endpoint was the change from baseline to month 18 in the modified Neuropathy Impairment Score +7 (mNIS+7), which assesses motor strength, reflexes, sensation, nerve conduction, and postural blood pressure.
    - Patients treated with Onpattro had a mean 6.0-point decrease (improvement) in mNIS+7 score from baseline compared to a mean 28.0-point increase (worsening) for patients in the placebo group, resulting in a mean 34.0-point difference relative to placebo, after 18 months of treatment ($p < 0.001$).
    - In addition, 56% of Onpattro-treated patients at month 18 experienced reversal of neuropathy impairment (as assessed by mNIS+7 score) relative to their own baseline, compared to 4% of patients who received placebo.
- Warnings and precautions of Onpattro include infusion-related reactions and reduced serum vitamin A levels and recommended supplementation.
- The most frequently reported adverse reactions (≥10% of Onpattro-treated patients and ≥ 3% more than placebo) were upper respiratory tract infections and infusion-related reactions.
- The recommended dose of Onpattro is 0.3 mg/kg for patients weighing less than 100 kg and 30 mg for patients weighing 100 kg or more, administered via intravenous infusion once every 3 weeks by a healthcare professional.
    - Dosing is based on actual body weight.
    - All patients should receive premedication with a corticosteroid, acetaminophen, and antihistamines prior to Onpattro to reduce the risk of infusion-related reactions.
    - Refer to the Onpattro drug label for additional dosing and administration details.
- Alnylam will provide ongoing support for Onpattro patients through the Alnylam Assist™ program, which includes financial assistance options, benefit verification and claims support, and ordering assistance and delivery facilitation. Patients will also have access to dedicated Case Managers and Patient Education Liaisons to provide personalized support throughout the treatment process.

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- Endpoints News reported that the list price of Onpattro has been set at $450,000 per year for the estimated 3,000 patients diagnosed with hATTR amyloidosis in the U.S. Alnylam announced they will be pursuing Value-Based Agreements with health insurers, with the goal that Alnylam will be paid based on the ability of Onpattro to deliver outcomes in the real world setting comparable to those demonstrated in clinical trials.

- Alnylam expects to have Onpattro available for shipment to healthcare providers in the U.S. within 48 hours. Onpattro will be available as a 10 mg/5 mL (2 mg/mL) single-dose vial.