Tegsedi™ (inotersen) – New orphan drug approval

- On October 5, 2018, Akcea Therapeutics and Ionis Pharmaceuticals announced the FDA approval of Tegsedi (inotersen), for treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults.

- 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.

- Tegsedi is an antisense oligonucleotide inhibitor of human transthyretin (TTR) protein synthesis. In hATTR amyloidosis, TTR protein misfolds and accumulates as amyloid deposits throughout the body. Tegsedi causes a reduction of serum TTR protein and TTR protein deposits in tissues.

- The efficacy of Tegsedi was demonstrated in a study of adult patients with polyneuropathy caused by hATTR amyloidosis. Patients were randomized to receive either Tegsedi (n = 113) or placebo (n = 60) for 65 weeks. The co-primary efficacy endpoints were the change from baseline to week 66 in the modified Neuropathy Impairment Scale+7 (mNIS+7) composite score (higher scores representing a greater severity of disease) and the Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score (higher scores representing greater impairment).

    - Patients treated with Tegsedi had a mean increase of 5.8 in the mNIS+7 score from baseline vs. a mean increase of 25.5 for patients in the placebo group (mean difference -19.7; 95% CI: -26.4, -13.0; $p < 0.001$).
    - Patients treated with Tegsedi had a mean increase of 1.0 in the Norfolk QoL-DN score from baseline vs. a mean increase of 12.7 for patients in the placebo group (mean difference -11.7; 95% CI: -18.3, -5.1; $p < 0.001$).

- Tegsedi carries a boxed warning for thrombocytopenia and glomerulonephritis.

- Tegsedi is contraindicated in patients with platelet counts < 100 x 10^9/L; history of acute glomerulonephritis caused by Tegsedi; and patients with a history of a hypersensitivity reaction to Tegsedi.

- Additional warnings and precautions of Tegsedi include stroke and cervicocephalic arterial dissection; inflammatory and immune effects; Tegsedi REMS program; liver effects; hypersensitivity reactions/antibody formation; uninterpretable platelet counts (reaction between antiplatelet antibodies and ethylenediaminetetra-acetic acid); and reduced serum vitamin A levels and supplementation.

- The most common adverse reactions (≥ 20% and more frequently than placebo) with Tegsedi use were injection site reactions, nausea, headache, fatigue, thrombocytopenia, and fever.

- The recommended dose of Tegsedi is 284 mg injected subcutaneously (SC) once weekly.

    - The first injection administered by the patient or caregiver should be performed under the guidance of an appropriately qualified healthcare professional.
    - SC injections should be administered in the abdomen, upper thigh region, or outer area of the upper arm.

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- Akcea has created Akcea Connect™, a patient support program made up of dedicated, regionally-based nurse case managers. This program offers free, private and personalized support to patients and their caregivers and families across the US.

- The reported list price for Tegsedi is $450,000 per year.

- Akcea's launch plans for Tegsedi are pending. Tegsedi will be available as 284 mg/1.5 mL single-dose prefilled syringes.

    — Tegsedi will only be available through a specialty pharmacy.