Spinraza™ (nusinersen) – New Orphan Drug Approval

- On December 23, 2016, Biogen announced the FDA approval of Spinraza (nusinersen) injection, for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients.
    - Spinraza is the first and only FDA-approved treatment available in the U.S. for SMA.
    - Spinraza was discovered and developed by Ionis and Biogen, and licensed to Biogen, who is responsible for future development, manufacturing, and commercialization.
- SMA is a rare, hereditary disease characterized by loss of motor neurons in the spinal cord and lower brain stem, and results in severe and progressive muscular atrophy and weakness. Individuals with the most severe type of SMA can become paralyzed and have difficulty performing the basic functions of life, such as breathing and swallowing.
    - SMA is caused by a loss of, or defect in, the survival motor neuron 1 (SMN1) gene, resulting in inadequate production of SMN protein. This protein is necessary for the proper maintenance of motor neurons.
    - The severity of SMA correlates with the amount of SMN protein. Type 1 SMA is the most severe life-threatening form. Patients with Type 2 or Type 3 SMA produce greater amounts of SMN protein and have less severe, but still life-threatening forms of SMA.
- Spinraza contains nusinersen, an antisense oligonucleotide. Through use of this technology, Spinraza has the potential to increase the amount of full-length SMN protein in patients with SMA.
- The safety and efficacy of Spinraza were demonstrated in a sham-procedure controlled trial in 121 symptomatic infantile-onset SMA patients, and was supported by open-label clinical trials conducted in pre-symptomatic and symptomatic SMA patients. The trial assessed the percentage of patients with improvement in motor milestones, such as head control, sitting, ability to kick in supine position, rolling, crawling, standing and walking.
    - More patients treated with Spinraza achieved improvement in motor milestones than the control group (40% vs. 0%, $p < 0.0001$).
    - In addition, the findings in the open-label, uncontrolled studies appeared generally supportive of the clinical efficacy demonstrated in the controlled clinical trial in infantile-onset patients.
- Warnings and precautions of Spinraza include thrombocytopenia and coagulation abnormalities, and renal toxicity.
- The most common adverse events (at least 20% of Spinraza-treated patients and at least 5% more frequently than in control patients) with Spinraza use were lower respiratory infection, upper respiratory infection, and constipation.
- Spinraza is to be administered intrathecally by, or under the direction of, healthcare professionals experienced in performing lumbar punctures. The recommended dose of Spinraza is 12 mg (5 mL) per administration given intrathecally.

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  - Initiate Spinraza treatment with 4 loading doses. The first three loading doses should be administered at 14-day intervals. The 4th loading dose should be administered 30 days after the 3rd dose. A maintenance dose should be administered once every 4 months thereafter.
  - Spinraza should be administered within 4 hours of removal from the vial.

- Biogen plans to launch Spinraza in approximately one week. Spinraza will be available as a 12 mg/5 mL single-dose vial for injection.