Ruzurgi™ (amifampridine) – New orphan drug approval

- On May 6, 2019, the FDA announced the approval of Jacobus' Ruzurgi (amifampridine), for the treatment of Lambert-Eaton myasthenic syndrome (LEMS) in patients 6 to less than 17 years of age.

- LEMS is a rare autoimmune disorder that affects the connection between nerves and muscles and causes weakness and other symptoms in affected patients. LEMS may be associated with other autoimmune diseases, but more commonly occurs in patients with cancer such as small cell lung cancer, where its onset precedes or coincides with the diagnosis of cancer.

    - LEMS can occur at any age. The prevalence of LEMS specifically in pediatric patients is not known, but the overall prevalence of LEMS is estimated to be three per million individuals worldwide.

- Ruzurgi is a broad spectrum potassium channel blocker; however, the mechanism by which Ruzurgi exerts its therapeutic effect in LEMS patients has not been fully elucidated.

- Amifampridine was also recently approved under the brand name Firdapse®. However, Firdapse is only approved for use in adult patients with LEMS.

    - Due to the orphan exclusivity granted to Catalyst Pharmaceuticals for Firdapse, Ruzurgi may not be finally approved for marketing in adult patients at this time. Orphan drug exclusivity blocks approval of any other application for the same drug for the same indication for 7 years.

- The efficacy of Ruzurgi was established in a double-blind study of 32 adult patients with LEMS. After an initial open-label run-in phase, patients were randomized to Ruzurgi or a switch to placebo. The primary measure of efficacy was the categorization of the degree of change (eg, greater than 30% deterioration) in the Triple Timed Up and Go test (3TUG) upon withdrawal of active medication, when compared with the time-matched average of the 3TUG assessments at baseline (higher 3TUG scores represent greater impairment).

    - None of the patients randomized to continue Ruzurgi experienced > 30% deterioration in the final post-dose 3TUG test. In contrast, 72% (13/18) of those randomized to placebo experienced > 30% deterioration in the final 3TUG test ($p < 0.0001$). Patients who were randomized to placebo returned to baseline after restarting Ruzurgi.

- The use of Ruzurgi in patients 6 to less than 17 years of age is supported by evidence from adequate and well-controlled studies of Ruzurgi in adults with LEMS, pharmacokinetic data in adult patients, pharmacokinetic modeling and simulation to identify the dosing regimen in pediatric patients, and safety data from pediatric patients 6 to less than 17 years of age.

- Ruzurgi is contraindicated in patients with a history of seizures or hypersensitivity to amifampridine or another aminopyridine.

- The most common adverse reactions (≥ 10% and at least 2% greater than placebo) with Ruzurgi use were paresthesia/dysesthesia, abdominal pain, dyspepsia, dizziness, and nausea.

- The recommended oral dosage for pediatric patients 6 to less than 17 years of age is dependent on body weight. Dosage should be increased based on clinical response and tolerability.

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Age and body weight	Initial dosage	Titration regimen	Maximum single dose	Maximum total daily dosage
Pediatric patients 6 to < 17 years of age weighing ≥ 45 kg	15 mg to 30 mg daily, in divided doses (2 to 3 times per day)	Increase daily in 5 mg to 10 mg increments, divided in up to 5 doses per day	30 mg	100 mg
Pediatric patients 6 to < 17 years of age weighing < 45 kg	7.5 mg to 15 mg daily, in divided doses (2 to 3 times per day)	Increase daily in 2.5 mg to 5 mg increments, divided in up to 5 doses per day	15 mg	50 mg

    - — When patients require a dosage in less than 5 mg increments, have difficulty swallowing tablets, or require feeding tubes, a 1 mg/mL suspension can be prepared.

- Jacobus' launch plans for Ruzurgi are pending. Ruzurgi will be available as a 10 mg functionally scored tablet.