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FDA approves eculizumab for generalized myasthenia gravis

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Yesterday the U.S. Food and Drug Administration (FDA) approved eculizumab as a treatment for adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive.

James F. Howard Jr., MD, Distinguished Professor of Neuromuscular Disease, professor of neurology, medicine and allied health, and chief of the Neuromuscular Disorders Section in the UNC School of Medicine, was lead investigator of the Phase 3 REGAIN study, which helped lead to FDA approval of the drug for the treatment of this chronic and debilitating neuromuscular disorder. It is the first new FDA-approved treatment for patients with gMG in more than 60 years.

"I am pleased that the FDA recognized the comprehensive clinical data supporting the benefits of Soliris for patients with anti-AChR antibody-positive gMG," Howard said. "It is exciting that patients who have not responded adequately to existing therapies will now have a new treatment option that was shown in clinical studies to improve patients' symptoms, their ability to carry out activities of daily living and their quality of life."

In the Phase 3 REGAIN study and its ongoing open-label extension study, eculizumab demonstrated treatment benefits for patients with anti-AChR antibody-positive gMG who had previously failed immunosuppressive treatment and continued to suffer from significant unresolved disease symptoms, which can include difficulties walking,

talking, swallowing and breathing. These patients are at an increased risk of disease exacerbations and crises that may require hospitalization and intensive care, and may be life-threatening. Such patients represent approximately 5-10 percent of the total MG patient population.

Results from the REGAIN study were published Friday (October 20, 2017) by *The Lancet Neurology*.

Eculizumab is manufactured by Alexion Pharmaceuticals, Inc. and sold under the name Soliris.

Chronic uncontrolled activation of the complement system, a part of the immune system, plays a major role in the debilitating symptoms and potentially life-threatening complications for patients with gMG who are anti-AChR antibody-positive. By selectively and effectively inhibiting the terminal complement cascade, eculizumab targets a critical underlying cause of the disease.

Myasthenia Gravis (MG) is a debilitating, chronic and progressive autoimmune neuromuscular disease that can occur at any age but most commonly begins for women before the age of 40 and men after the age of 60. It typically begins with weakness in the muscles that control the movements of the eyes and eyelids, and often progresses to the more severe and generalized form, known as gMG, with weakness of the head, neck, trunk, limb and respiratory muscles.

While most patients with gMG can be managed with current therapies for MG, 10-15 percent of patients fail to respond adequately to or cannot tolerate multiple therapies for MG, and continue to suffer profound muscle weakness and severe disease symptoms that limit function. These patients can suffer from slurred speech, choking, impaired swallowing, double or blurred vision, disabling fatigue, immobility requiring assistance, shortness of breath, and episodes of

respiratory failure. Complications, exacerbations and myasthenic crises can require hospital and intensive care unit admissions with prolonged stays, and can be life-threatening.

In patients with anti-AChR antibody-positive MG, the body's own immune system turns on itself to produce antibodies against AChR, a receptor located on muscle cells at the neuromuscular junction (NMJ) and used by nerve cells to communicate with the muscles these nerves control. The binding of these antibodies to AChR activates the complement cascade, another part of the immune system, which leads to a localized destruction of the muscle membrane at the NMJ. As a result, the communication between nerve and muscle is impaired, which in turn leads to a loss of normal muscle function.

Patients with AChR antibody-positive gMG who continue to suffer from severe disease symptoms and complications despite current therapies for MG represent approximately 5-10 percent of all patients with MG.

More information: James F Howard et al. Safety and efficacy of eculizumab in anti-acetylcholine receptor antibody-positive refractory generalised myasthenia gravis (REGAIN): a phase 3, randomised, double-blind, placebo-controlled, multicentre study, *The Lancet Neurology* (2017). DOI: 10.1016/S1474-4422(17)30369-1

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