New periodic paralysis drug

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More than 15 years of research led by neurologists at the University of Rochester Medical Center (URMC) has culminated in the first approved treatment for individuals with a rare neuromuscular disorder called periodic paralysis. The U.S. Food and Drug Administration (FDA) recently approved dichlorphenamide, which is being marketed under the brand name Keveyis by Taro Pharmaceuticals, for individuals with the disease.

Periodic paralysis is extremely rare - an estimated 5,000 people in the U.S. suffer from the disease - and the condition is generally neither fatal nor life shortening, but can have a significant impact on quality of life depending upon the frequency and severity of the paralytic "attacks" that are the hallmark of the disease. Some patients can go months without an

attack and may only experience limited movement in an extremity, while others experience attacks daily and can be immobilized for several hours at a time. Over time, many patients become weaker.

"This is one of the most dramatic diseases in medicine," said Robert "Berch" Griggs, M.D., a professor in the University of Rochester Medical Center Department of Neurology and principal investigator of the clinical studies that led to the drug's approval. "A patient can wake up in the morning and be completely paralyzed from the neck down. Over the course of hours they regain mobility so by the time they get the doctor's office they are often completely normal."

Griggs is an internationally recognized expert in periodic paralysis and is sought out by patients from around the world. Almost 45 years ago, Griggs first demonstrated that the drug acetazolamide was partially effective in treating periodic paralysis and, more recently, was part of a team of researchers that discovered the genetic cause of periodic paralysis. In 2003, the National Institutes of Health tapped Griggs to head a national network of physicians and scientists that are focusing on rare neurological disorders such as periodic paralysis.

URMC's role in bringing dichlorphenamide to market began in 2000, when Griggs and his colleague Rabi Tawil, M.D. showed in a small study that dichlorphenamide was highly effective in preventing the attacks and keeping patients' muscle strong.

Dichlorphenamide had been approved by the FDA for the treatment of glaucoma, but the drug's original manufacturer, Merck & Co., had taken it off the market. The results of the 2000 study prompted Taro Pharmaceuticals to purchase the license for the drug from Merck in order to make it available for the periodic paralysis study.

A larger study involving dichlorphenamide was launched in 2004. The

HypHop clinical trial - named after the two types of the disease under investigation: hyperkalemic and hypokalemic periodic paralysis - involved 65 patients and confirmed the findings of the earlier study.

Periodic paralysis is a channelopathy; a family of genetic diseases in which the channels - or gates - that control the movement of ions in cells do not function properly. The precise and timely regulation of these ions, such as sodium, calcium, potassium and chloride, are critical to muscle control. When the movement of ions in our muscles and other tissues is off by just a tiny bit, the result is disease. Hypokalemic and hyperkalemic periodic paralysis are disorders of the sodium and calcium channels.

"For those living with often debilitating symptoms, the approval of Keveyis is both an important and much needed treatment advance and an opportunity for greater disease awareness and understanding, something that has long been a challenge for these people," said Griggs.

Provided by University of Rochester Medical Center