Mallinckrodt Announces Inclusion of Acthar® Gel (Repository Corticotropin Injection) in New European Respiratory Society (ERS) Treatment Guidelines for Patients with Pulmonary Sarcoidosis

July 1, 2021

-- Along with a Sarcoidosis Expert Panel Consensus Statement previously published in European Respiratory Review, the ERS guidelines support the use of Acthar Gel in the management of certain patients with symptomatic pulmonary sarcoidosis --

-- Guidelines are the first ERS-issued evidence-based clinical practice recommendations for sarcoidosis treatment to include Acthar Gel --

DUBLIN, July 1, 2021 /PRNewswire/ -- Mallinckrodt plc (OTCMKTS: MNKKQ), a global biopharmaceutical company, today announced new treatment guidelines for sarcoidosis from the European Respiratory Society (ERS), which include use of Acthar® Gel (repository corticotropin injection) therapy in the clinical management of certain patients with pulmonary sarcoidosis, published in *European Respiratory Journal*.[1] The treatment guidelines are the first ERS-issued evidence-based clinical practice recommendations, aimed at providing guidance to physicians treating sarcoidosis patients, to include Acthar Gel. In addition, the guidelines support existing consensus recommendations on the use of Acthar Gel in the management of patients with pulmonary sarcoidosis based on a recent U.S. Sarcoidosis Expert Panel Consensus Statement, previously published in *European Respiratory Review*.[2]

Acthar Gel is approved by the U.S. Food and Drug Administration (FDA) for the treatment of symptomatic sarcoidosis and is only commercially available in the U.S.[3] Please see Important Safety Information for Acthar Gel below.

The guidelines—developed by aERS Task Force committee composed of clinicians, methodologists and patient advocates with experience in sarcoidosis—list Acthar Gel among the various anti-inflammatory treatments for pulmonary sarcoidosis and note it can be used on a case-by-case basis when other therapies are ineffective or not tolerated. Additionally, the guidelines state that recent studies have suggested the effectiveness of Acthar Gel as a steroid-sparing agent in advanced sarcoidosis. The guidelines acknowledge that the potential mechanisms of action of Acthar Gel have not been fully elucidated and that its understanding has continued to evolve with further research.[1] Mallinckrodt continues to invest in studies to advance the characterization of the proposed mechanisms of action and to better understand the efficacy and safety profiles of Acthar Gel.

"Sarcoidosis is a multisystem disorder that almost always affects the lungs. The condition can be debilitating for many patients and in some cases become serious or life-threatening, which is why it is important to recognize those patients with progressive disease and manage them appropriately," said **Robert Baughman, M.D., Pulmonologist at University of Cincinnati Health, lead author of the ERS guidelines and contributing author of the U.S. Sarcoidosis Expert Panel Consensus Statement**. "The new ERS guidelines, along with the expert panel consensus statement, provide practical guidance to physicians of the role of Acthar Gel in the clinical management of sarcoidosis based on the combined clinical experience of experts in the field, creating consensus around the real-world use of Acthar Gel in treating patients with this disease."

The U.S. Sarcoidosis Expert Panel Consensus Statement published in *European Respiratory Review* includes guidance on dosage, concomitant medications and adverse event (AE) management of advanced sarcoidosis with Acthar Gel. The panel, comprised of 12 independent physicians with expertise in treating patients with sarcoidosis, recommended a starting dose of Acthar Gel 40 units twice a week for most patients with less severe disease, but did not achieve consensus on whether a higher initial dose was indicated for patients with a more severe condition. In addition, Acthar Gel should be continued at a maintenance dose for most patients who respond to therapy, particularly those with chronic refractory/advanced sarcoidosis, and the maintenance dose should be individualized for each patient. If patients develop major adverse events, the recommendations suggested considering reducing or discontinuing Acthar Gel. The panel also made recommendations related to discontinuation of therapy, including weaning to the lowest efficacious dose if the patient has stable, well-controlled disease after six to 12 months of therapy.[2]

Study limitations include the following: There are no generally accepted criteria for consensus. The study is based on a degree of consensus, which may be refuted by future rigorous studies. Panelists were not accountable for their responses, and opinions may

be based on insufficient/minimal consideration. Panel selection and questionnaire development may introduce bias, and perspectives from stakeholders other than U.S.-based physicians may have been missed.

Regarding the use of concomitant medications, the panel recommended that concomitant steroids be tapered and potentially discontinued as quickly as possible in patients receiving Acthar Gel, but concomitant use of immunosuppressive medications should be continued. Consensus recommendations were also reached for AE management, including that Acthar Gel be titrated down or discontinued if other interventions fail or if AEs are severe and significant.[2]

"There has been a need for quite some time for evidence-based consensus on the treatment of sarcoidosis, a rare disease that can significantly impact patients' functioning and quality of life and can be difficult to diagnose and treat," said **Steven Romano, M.D., Executive Vice President and Chief Scientific Officer at Mallinckrodt**. "The ERS guidelines will help fill knowledge gaps in clinical care and enable more standardized treatment of symptomatic sarcoidosis to help improve clinical outcomes for patients. Moreover, both the guidelines and the sarcoidosis expert panel consensus statement provide practical, expert guidance on the use of Acthar Gel for physicians who manage patients with this complex disease."

Mallinckrodt has a dedicated team to support healthcare providers and patients throughout a patient's treatment regimen including personalized injection training.

About Sarcoidosis

Sarcoidosis is a challenging, yet manageable, rare multisystem disease.[4,5] In some cases the symptoms may come and go throughout one's lifetime. This is referred to as symptomatic sarcoidosis. In people living with sarcoidosis, the immune system overreacts, forming clumps of cells called granulomas that result in inflammation of the body's tissues.[6] The disease can impact any organ but most often impacts the lungs, lymph nodes, eyes, and skin.[4] Over 90 percent of people with sarcoidosis suffer lung problems.[6] Concomitant involvement of organs outside of the lungs is common, occurring in as many as half of all sarcoidosis cases.[7]

IMPORTANT SAFETY INFORMATION

Contraindications

Acthar is contraindicated:

- For intravenous administration
- In infants under 2 years of age who have suspected congenital infections
- With concomitant administration of live or live attenuated vaccines in patients receiving immunosuppressive doses of Acthar
- In patients with scleroderma, osteoporosis, systemic fungal infections, ocular herpes simplex, recent surgery, history of or the presence of a peptic ulcer, congestive heart failure, uncontrolled hypertension, primary adrenocortical insufficiency, adrenocortical hyperfunction, or sensitivity to proteins of porcine origin

Warnings and Precautions

- The adverse effects of Acthar are related primarily to its steroidogenic effects
- Acthar may increase susceptibility to new infection or reactivation of latent infections
- Suppression of the hypothalamic-pituitary-adrenal (HPA) axis may occur following prolonged therapy with the potential for adrenal insufficiency after withdrawal of the medication. Adrenal insufficiency may be minimized by tapering of the dose when discontinuing treatment. During recovery of the adrenal gland patients should be protected from the stress (e.g., trauma or surgery) by the use of corticosteroids. Monitor patients for effects of HPA axis suppression after stopping treatment
- Cushing's syndrome may occur during therapy but generally resolves after therapy is stopped. Monitor patients for signs and symptoms
- Acthar can cause elevation of blood pressure, salt and water retention, and hypokalemia. Monitor blood pressure and sodium and potassium levels
- Acthar often acts by masking symptoms of other diseases/disorders. Monitor patients carefully during and for a period following discontinuation of therapy
- Acthar can cause gastrointestinal (GI) bleeding and gastric ulcer. There is also an increased risk for perforation in patients with certain GI disorders. Monitor for signs of perforation and bleeding
- Acthar may be associated with central nervous system effects ranging from euphoria, insomnia, irritability, mood swings, personality changes, and severe depression to psychosis. Existing conditions may be aggravated
- Patients with comorbid disease may have that disease worsened. Caution should be used when prescribing Acthar in patients with diabetes and myasthenia gravis
- Prolonged use of Acthar may produce cataracts, glaucoma, and secondary ocular infections. Monitor for signs and symptoms
- Acthar is immunogenic and prolonged administration of Acthar may increase the risk of hypersensitivity reactions. Neutralizing antibodies with chronic administration may lead to loss of endogenous ACTH and Acthar activity
- There may be an enhanced effect in patients with hypothyroidism and in those with cirrhosis of the liver

- Long-term use may have negative effects on growth and physical development in children. Monitor pediatric patients
- Decrease in bone density may occur. Bone density should be monitored in patients on long-term therapy
- Pregnancy Class C: Acthar has been shown to have an embryocidal effect and should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus

Adverse Reactions

- Commonly reported postmarketing adverse reactions for Acthar include injection site reaction, asthenic conditions (including fatigue, malaise, asthenia, and lethargy), fluid retention (including peripheral swelling), insomnia, headache, and blood glucose increased
- The most common adverse reactions for the treatment of infantile spasms (IS) are increased risk of infections, convulsions, hypertension, irritability, and pyrexia. Some patients with IS progress to other forms of seizures; IS sometimes masks these seizures, which may become visible once the clinical spasms from IS resolve

Other adverse events reported are included in the full Prescribing Information.

Please see full Prescribing Information for additional Important Safety Information.

ABOUT MALLINCKRODT

Mallinckrodt is a global business consisting of multiple wholly owned subsidiaries that develop, manufacture, market and distribute specialty pharmaceutical products and therapies. The company's Specialty Brands reportable segment's areas of focus include autoimmune and rare diseases in specialty areas like neurology, rheumatology, nephrology, pulmonology and ophthalmology; immunotherapy and neonatal respiratory critical care therapies; analgesics and gastrointestinal products. Its Specialty Generics reportable segment includes specialty generic drugs and active pharmaceutical ingredients. To learn more about Mallinckrodt, visit www.mallinckrodt.com.

Mallinckrodt uses its website as a channel of distribution of important company information, such as press releases, investor presentations and other financial information. It also uses its website to expedite public access to time-critical information regarding the company in advance of or in lieu of distributing a press release or a filing with the U.S. Securities and Exchange Commission (SEC) disclosing the same information. Therefore, investors should look to the Investor Relations page of the website for important and time-critical information. Visitors to the website can also register to receive automatic e-mail and other notifications alerting them when new information is made available on the Investor Relations page of the website.

CAUTIONARY STATEMENTS RELATED TO FORWARD-LOOKING STATEMENTS

This release includes forward-looking statements concerning Acthar Gel including its potential impact on patients and anticipated benefits associated with its use, as well as related on-going studies. The statements are based on assumptions about many important factors, including the following, which could cause actual results to differ materially from those in the forward-looking statements: satisfaction of regulatory and other requirements; actions of regulatory bodies and other governmental authorities; changes in laws and regulations; issues with product quality, manufacturing or supply, or patient safety issues; and other risks identified and described in more detail in the "Risk Factors" section of Mallinckrodt's most recent Annual Report on Form 10-K and other filings with the SEC, all of which are available on its website. The forward-looking statements made herein speak only as of the date hereof and Mallinckrodt does not assume any obligation to update or revise any forward-looking statement, whether as a result of new information, future events and developments or otherwise, except as required by law.

CONTACT

Media Inquiries
Caren Begun
Green Room Communications
201-396-8551
caren@greenroompr.com

Investor Relations
Daniel J. Speciale
Vice President, Finance and Investor Relations Officer
314-654-3638
daniel.speciale@mnk.com

Government Affairs
Mark Tyndall
Senior Vice President, US General Counsel & Government Affairs
mark.tyndall@mnk.com

References

[1] Baughman RP, Valeyre D, Korsten P, et al. ERS clinical practice guidelines on treatment of sarcoidosis. *Eur Respir J*. 2021, 2004079; DOI: 10.1183/13993003.04079-2020.
[2] Rahaghi FF, Sweiss NJ, Saketkoo LA, et al. Management of repository corticotrophin injection therapy for pulmonary sarcoidosis: a Delphi study. *Eur Respir Rev*. 2020;29:190147. https://doi. org/10.1183/16000617.0147-2019.
[3] Acthar® Gel (repository corticotropin injection) [prescribing information]. Mallinckrodt ARD LLC.
[4] Judson MA. The clinical features of sarcoidosis: a comprehensive review. *Clin Rev Allerg Immunol*. 2015;49:63-78.
[5] Baughman RP, Field S, Costabel U, et al. Sarcoidosis in America. Analysis based on health care use. *Ann Am Thorac Soc*. 2016;13:1244-1252.
[6] Baughman RP, Culver DA, Judson MA. A concise review of pulmonary sarcoidosis. *Am J Respir Crit Care Med*. 2011;183:573-581.
[7] Shigemitsu H, Patel HV, Schreiber MP. Extrapulmonary sarcoidosis. In: Judson MA, ed. Pulmonary Sarcoidosis: A Guide for the Practicing Clinician. Vol 17. New York, NY: Springer; 2014:149-186.

View original content to download multimedia:https://www.prnewswire.com/news-releases/mallinckrodt-announces-inclusion-of-acthar-gel-repository-corticotropin-injection-in-new-european-respiratory-society-ers-treatment-guidelines-for-patients-with-pulmonary-sarcoidosis-301324261.html

SOURCE Mallinckrodt plc