Mallinckrodt Announces Journal Publication of Real-World Data on Acthar® Gel (repository corticotropin injection) to Treat Symptomatic Sarcoidosis in African American and Non-African American Patients

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– Retrospective analysis suggests Acthar Gel treatment was associated with similar improvement in health status and overall symptom reduction in African Americans and non-African Americans with symptomatic sarcoidosis[1] –

– Findings on treatment response and physician-reported outcomes indicate that Acthar Gel may be a viable treatment option for both African American and non-African American sarcoidosis patients[1] –

DUBLIN, March 11, 2024 /PRNewswire/ -- Mallinckrodt plc, a global specialty pharmaceutical company, today announced the publication of findings from a retrospective chart review of Acthar® Gel (repository corticotropin injection) treatment outcomes for African American and non-African American patients with symptomatic sarcoidosis – including treatment patterns, co-medication use, and overall health outcomes.[1] This analysis suggested that Acthar Gel treatment was associated with similar improvements in health outcomes, a reduction in symptoms, and reduced co-medication use in both African Americans and non-African Americans with symptomatic sarcoidosis.[1] The manuscript was recently published online in *Therapeutics & Clinical Risk Management*.

This research builds upon findings from a study investigating the clinical and real-world outcomes of Acthar Gel treatment in a subgroup of African Americans with symptomatic sarcoidosis, previously presented at the 2022 American Thoracic Society Annual International Conference in San Francisco, CA, and published in *Therapeutic Advances in Respiratory Disease* in 2019.[2]

Acthar is a naturally sourced complex mixture of adrenocorticotropic hormone analogs and other pituitary peptides.[3] Acthar Gel is approved by the U.S. Food and Drug Administration (FDA) for the treatment of several autoimmune disorders and medical conditions known to cause inflammation, including symptomatic sarcoidosis.[3]

Please see additional indications and Important Safety Information below.

"The results of this retrospective medical chart review highlight unmet needs that exist for African American patients with symptomatic sarcoidosis, who are disproportionately affected by the disease, and reinforce Acthar Gel's potential to help improve health outcomes for appropriate patients,"[1,4,5] said **George Wan, Ph.D., M.P.H., Vice President, Evidence Generation and Data Sciences, Mallinckrodt.** "This research reflects Mallinckrodt's commitment to collecting real-world data on the relationship between patient characteristics, treatment patterns, and outcomes to support clinicians' treatment decisions and address disparities in symptomatic sarcoidosis care."[1]

About the Study:[1]

In this retrospective analysis, a national database of Acthar Gel prescribers and the American Medical Association Physician Masterfile listing were merged to obtain a sample of 98 physicians to provide data on the last 6 consecutive patients seen who met the study's eligibility criteria. The medical records were extracted for adult patients (≥18 years) with a diagnosis of advanced symptomatic sarcoidosis, who had ≥1 symptom, and who had either completed at least one course of Acthar Gel or had received Acthar Gel for at least 6 months during data collection.

A total of 272 patients with symptomatic sarcoidosis were included in this analysis (African American (AA): n=168; non-African American (non-AA): n=104). Most patients in both race groups were diagnosed with stage 3 or 4 sarcoidosis based on chest imaging and biopsy (AA: 61.3%, n=103 vs. non-AA: 68.3%, n=71; p=0.2453).

Per an assessment of patient characteristics and Acthar Gel treatment patterns, this analysis suggests that the average time since the first diagnosis of sarcoidosis was slightly longer among AA than non-AA (mean ± SD: 5.2 ± 7.6 years vs. 4.3 ± 5.1 years; p>0.05).[1] Further, a lower proportion of AA vs. non-AA had completed a course of Acthar Gel therapy (44%, n=74 vs. 55.8%, n=58; p=0.0602) during the data collection period,[1] and the duration of Acthar Gel treatment was slightly longer among AA vs. non-AA (mean ± SD: 31.7 ± 32 vs. 29 ± 27.4 weeks; p>0.05).[1]

"This research underscores the importance of conducting real-world studies to provide data that helps to recognize the disparities in symptomatic sarcoidosis care and address unmet needs to better support health outcomes for all appropriate patients," said **Mary McGowan, Chief Executive Officer, Foundation for Sarcoidosis Research (FSR)**. FSR is the leading international organization dedicated to finding a cure for sarcoidosis and

improving care for sarcoidosis patients through research, education, and support.

Key Findings:

Co-Medication Utilization Patterns[1]

- Significantly fewer patients among both race groups were on any co-medication after Acthar Gel initiation (p<0.0001):
  - AA before: 88.1%, n=148 vs. after: 20.2%, n=34
  - Non-AA before: 83.7%, n=87 vs. after: 24%, n=25

- More AA had a reduction in any co-medication use after Acthar Gel initiation (AA: -77% vs. non-AA: -71%; p<0.0001).
  - After Acthar Gel initiation, fewer AA (before: 59.5%, n=100 vs. after: 11.9%, n=20; p<0.0001) and non-AA (before: 65.4%, n=68 vs. after: 14.4%, n=15; p<0.0001) were on glucocorticoids.
  - Overall, the mean prednisone dose reduced after Acthar Gel initiation among AA (before: 18.5 mg/day vs. after: 10.1 mg/day) and non-AA (before: 17.6 mg/day vs. after: 10 mg/day).
  - The proportion of patients on prednisone daily dose of <10 mg increased after Acthar Gel initiation among both race groups (AA before: 27.8%, n=27/97 vs. after: 31.6%, n=6/19; non-AA before: 13.6%, n=9/66 vs. after: 60%, n=9/15).

Physicians' Assessment of Improvement[1]

- The health status of 95.2% (n=160) of AA and 97.1% (n=101) of non-AA improved following treatment with Acthar Gel, based on physician-provided assessments of patient outcomes. Treatment response to overall symptoms was not statistically significantly different between both race groups (AA: 72.6%, n=122 vs. non-AA: 70.2%, n=73)
- The most frequently reported changes in symptoms following Acthar Gel treatment in both race groups were:
  - Reduction in inflammation (AA: 33.9%, n=57 vs. non-AA: 32.7%, n=34)
  - Improvement in quality of life (AA: 31.5%, n=53 vs. non-AA: 34.6%, n=36)
  - Improvement in lung function (AA: 30.4%, n=51 vs. non-AA: 53.8%, n=56; p<0.05)
  - Reduction in fatigue (AA: 27.4%, n=46 vs. non-AA: 35.6%, n=37)

Limitations:[1]

Data retrospectively collected from medical charts of patients may have omissions and errors. Completeness of information was assessed to the extent possible to minimize bias resulting from any missing data. In addition, only data available in medical charts or known to be complete to the respondents were extracted. Additional limitations of this study include:

- Physicians' standards for the interpretation of change in each patient's health status vary which may result in bias due to over- or under-estimation of the effectiveness of Acthar Gel.
- This study was unable to quantify clinical data such as diagnostic and safety measures, clinical and sustained response after treatment, and reasons for discontinuation or dose adjustments related to Acthar Gel.
- Due to the exploratory nature of this analysis, data were not collected for other medications besides Acthar Gel.
- Data on adverse reactions in this population, drivers of the decision to use Acthar Gel, and detailed information on prior therapies were not captured.

This study was sponsored by Mallinckrodt Pharmaceuticals.

INDICATIONS

Acthar Gel is indicated for:

- Inducing a diuresis or a remission of proteinuria in nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus
- Monotherapy for the treatment of infantile spasms in infants and children under 2 years of age
- Treatment of acute exacerbations of multiple sclerosis in adults. Controlled clinical trials have shown Acthar to be effective in speeding the resolution of acute exacerbations of multiple sclerosis. However, there is no evidence that it affects the ultimate outcome or natural history of the disease
- Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, anterior segment inflammation
- Symptomatic sarcoidosis
- Treatment during an exacerbation or as maintenance therapy in selected cases of systemic lupus erythematosus
- Treatment during an exacerbation or as maintenance therapy in selected cases of dermatomyositis (polymyositis)
- Adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in: psoriatic arthritis; rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy); ankylosing spondylitis

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 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. Cases of anaphylaxis have been reported in the postmarketing setting. 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

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

Pregnancy

- Acthar may cause fetal harm when administered to a pregnant woman

Please see full Prescribing Information for additional Important Safety Information.

ABOUT SYMPTOMATIC SARCOIDOSIS

Sarcoidosis is a challenging and rare multisystem disease.[6] In some cases, the symptoms may come and go throughout a lifetime.[6] This is referred to as symptomatic sarcoidosis.[6] In people with sarcoidosis, the immune system overreacts, forming clumps of cells called granulomas that result in inflammation to the body's tissues.[7] The disease can impact any organ, but it most often impacts the lungs, lymph nodes, eyes, liver, and skin.[8] Nearly 90 percent of people with sarcoidosis will suffer lung problems.[8] Concomitant involvement of organs outside of the lungs is common, occurring in more than half of all sarcoidosis cases, according to one study.[2]

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, hepatology, nephrology, pulmonology, ophthalmology, and oncology; 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.

CAUTIONARY STATEMENTS RELATED TO FORWARD-LOOKING STATEMENTS

This release contains forward-looking statements, including with regard to Acthar® Gel, its potential to improve health and treatment outcomes, its potential impact on patients. 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: the effects of Mallinckrodt's recent emergence from bankruptcy; satisfaction of, and compliance with, 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 or adverse side effects or adverse reactions associated with Acthar Gel; 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.

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References

[1] Bindra J, et al. Acthar Gel in African Americans versus Non-African Americans with Symptomatic Sarcoidosis: Physician Assessment of Patient Medical Records. *Ther Clin Risk Manag*. 2024;20:83-94 https://doi.org/10.2147/TCRM.S438174.

[2]Chopra I, et al. Repository Corticotropin Injection in Patients with Advanced Symptomatic Sarcoidosis: Retrospective Analysis of Medical Records. *Ther Adv Res Dis*. 2019(13);1-11. DOI: 10.1177/1753466619888127.

[3] Acthar® Gel (repository corticotropin injection) [prescribing information]. Mallinckrodt ARD LLC. 2023.

[4] Judson MA. Pulmonary Sarcoidosis: A Guide for the Practicing Clinician. *Humana Press, New York, NY.* 2014. 8;149-186.

[5] Hena, K. M. Sarcoidosis Epidemiology: Race Matters. *Front Immunol*. 2020;11:1-5.

[6] Sarcoidosis. American College of Chest Physicians. Available at: http://chestnet.org/sarcoid. Accessed February 2024.

[7] Sarcoidosis Overview. 2019. Cleveland Clinic. Available at: https://my.clevelandclinic.org/health/diseases/11863-sarcoidosis-overview. Accessed February 2024.

[8] Judson MA, Boan AD, Lackland DT. The Clinical Course of Sarcoidosis: Presentation, Diagnosis, and Treatment in a Large White and Black Cohort in the United States. *Sarcoidosis Vasc Diffuse Lung Dis*. 2012. 29(2);119-127.

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