Mallinckrodt Presents Latest Health Economics Data on Acthar® Gel (Repository Corticotropin Injection) at the Academy of Managed Care Pharmacy (AMCP) Nexus 2023

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-- Findings from two health economics analyses of Acthar Gel provide further insight into its cost-effectiveness as a treatment option for advanced symptomatic sarcoidosis,[1] and its impact on clinical, economic, and real-world outcomes in patients with nephrotic syndrome[2] --

DUBLIN, Oct. 26, 2023 /PRNewswire/ -- Mallinckrodt plc (OTCMKTS: MNKTQ), a global specialty pharmaceutical company, recently shared findings from Mallinckrodt's latest health economics outcomes research on Acthar® Gel (repository corticotropin injection) for patients with advanced symptomatic sarcoidosis and nephrotic syndrome (NS)[1,2] at the Academy of Managed Care Pharmacy (AMCP) Nexus 2023 in Orlando, FL October 16-19, 2023.

A full list of accepted abstracts presented at AMCP Nexus 2023 can be found here.

Acthar is a naturally sourced complex mixture of adrenocorticotropic hormone analogs and other pituitary peptides. 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.[3]

Please see indications and Important Safety Information below.

In a poster (D20) titled "Cost-Effectiveness of Acthar Gel versus Standard of Care for the Treatment of Advanced Symptomatic Sarcoidosis," results were presented from a cost-effectiveness analysis of Acthar Gel and the standard of care (SoC) treatments over two and three years in patients with advanced symptomatic sarcoidosis in the U.S.[1] In this analysis, a probabilistic cohort-level state-transition approach was used. Patients were monitored at the end of a three-month cycle for a partial or complete response. Clinical parameters and health utility data were sourced from the PULSAR trial (NCT03320070) and healthcare utilization, costs, and disutilities were sourced from the published literature.[1]

- From the payer perspective – including treatment and direct medical costs – the findings of this analysis showed that Acthar Gel versus SoC resulted in an incremental cost-effectiveness ratio (ICER) of $134,796 per quality-adjusted life-year (QALY) and $39,179 per QALY over two and three years, respectively.
- From a societal perspective – including treatment, direct medical and indirect (caregiving, productivity loss, work-related training) costs – Acthar versus SoC resulted in an ICER of $117,622 per QALY over two years and $21,967 per QALY over three years.

Model inputs used in the analysis were derived or extrapolated from the PULSAR clinical trial or published literature, which may not reflect real-world experience or may result in under- or over-estimation of results. The simplified care paradigm used for the model may not capture the complexity of sarcoidosis. Clinical response was based on composite sarcoidosis treatment scores, which might result in variation in cost-effectiveness estimates.

The full data manuscript from this study was published in *ClinicoEconomics and Outcomes Research* on October 17, 2023.

Additionally, a poster (N1) titled "Nephrotic Syndrome: Patient Characteristics, Treatment Patterns, and Related Outcomes After Treatment with Acthar Gel or Comparable Standard of Care in a Large Administrative Claims Database" detailed results from a retrospective, observational cohort study characterizing patients with NS who initiated Acthar or other therapies used after corticosteroids or calcineurin inhibitors.[2] In this study, treatment for NS with Acthar for proteinuria and other treatments (azathioprine, chlorambucil, cyclophosphamide, mycophenolate mofetil, or rituximab) was analyzed via a large commercial claims database (Symphony Health). Patients had a confirmed diagnosis for NS, were 18 years of age or older, and had 12 months of continuous enrollment pre- and post-index.[2]

- In this analysis, after treatment with Acthar Gel, there was a significant reduction in the proportion of patients (n=315) taking corticosteroids (66%; n=209 vs. 51%; n=162, p<0.001), patients on extended use (≥60 days) of corticosteroids (37%; n=117 to 25%; n=80, p<0.001), and the average daily patient dose of corticosteroids (32.1 ± 21.3 to 21.7 ± 21.1, p=0.001) compared to baseline.
- The Acthar Gel cohort had an increase in patients on dialysis (6%; n=20 to 14%; n=45, p<0.001), but no change was reported in renal transplants (10%; n=30 to 10%; n=32, p=0.774) or transplant complications (6%; n=18 to 6%; n=19,

p=1.000). The comparator cohort of patients taking other therapies (n=6,812) had fewer patients on dialysis (16%; n=1,105 to 12%; n=823, p<0.001), but an increase in renal transplants (19%; n=1,315 to 22%; n=1,475, p<0.001) and transplant complications (8%; n=547 to 10%; n=681, p<0.001).

"We are pleased to have shared our latest health economics research on Acthar Gel. These data further our understanding of treatment cost-effectiveness, clinical impact, and real-world outcomes for patients with conditions like symptomatic sarcoidosis and nephrotic syndrome,"[1,2] said **George Wan, Ph.D., M.P.H., Vice President, Evidence Generation and Data Sciences, Mallinckrodt.** "Acthar has a robust history of clinical evidence and experience, and we are committed to providing the medical community with the most up to date research to support its availability, use, and potential to improve outcomes for autoimmune and chronic inflammatory conditions across a range of FDA-approved indications."

Data collected in retrospective analyses and health economics models may have errors or omissions. Outcomes may be influenced by therapies not evaluated in the study and the clinical/health economics outcomes may not be solely attributable to Acthar.

These studies were funded by Mallinckrodt Pharmaceuticals.

ABOUT PROTEINURIA IN NEPHROTIC SYNDROME (NS)

NS is a collection of symptoms that occur when the blood vessels in the kidney begin to leak excess protein in the urine, a condition called proteinuria.[4] A variety of diseases and underlying disorders damage the kidneys and cause proteinuria in people with NS.[4] These etiologies can include glomerular diseases such as: idiopathic membranous nephropathy, focal segmental glomerulosclerosis, minimal change disease, membranoproliferative glomerulonephritis, lupus nephritis, and IgA nephropathy.[4,5,6,7,8,9] In these and other related disorders, the glomeruli, or small blood vessels that work as the kidney's filtering system, are damaged.[4]

Proteinuria is one of the most important adverse prognostic factors for progression to end stage renal failure in patients with glomerular disease. One of the goals of treating NS includes reducing or eliminating proteinuria.[10]

ABOUT SYMPTOMATIC SARCOIDOSIS

Sarcoidosis is a challenging and rare multisystem disease.[11] In some cases, the symptoms may come and go throughout a lifetime.[11] This is referred to as symptomatic sarcoidosis.[11] In people with sarcoidosis, the immune system overreacts, forming clumps of cells called granulomas that result in inflammation to the body's tissues.[12] The disease can impact any organ, but it most often impacts the lungs, lymph nodes, eyes, and skin.[13] Nearly 90 percent of people with sarcoidosis will suffer lung problems. Concomitant involvement of organs outside of the lungs is common, occurring in more than half of all sarcoidosis cases, according to one study.[14]

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 theses 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 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 segments 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; cultured skin substitutes 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 contains forward-looking statements, including with regard to Acthar® Gel, its potential to improve health and treatment outcomes, and 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 impact of Mallinckrodt's pending Chapter 11 cases; 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; 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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