Mallinckrodt Analysis Suggests Acthar® Gel (Repository Corticotropin Injection) May be a Cost-Effective Option Compared to Other Late-Line, Adult Treatments for Multiple Sclerosis Relapse

September 13, 2019

-- Retrospective Findings Presented at the 35th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) and 24th Annual Conference of Rehabilitation in Multiple Sclerosis --

STAINES-UPON-THAMES, United Kingdom, Sept. 13, 2019 /PRNewswire/ -- Mallinckrodt plc (NYSE: MNK), a global biopharmaceutical company, today announced findings from a retrospective analysis of Acthar® Gel (repository corticotropin injection) that showed the cost per response of Acthar Gel when used as a late-line treatment was lower than other late-line treatments, including plasmapheresis (PMP) and intravenous immunoglobulin (IVIg), for multiple sclerosis (MS) relapses in adults. In the analysis, response was defined as no additional relapse treatments or procedures within 30 days, and cost of care was defined to include MS-related inpatient and outpatient treatment and medication costs.

Acthar Gel is U.S. Food and Drug Administration (FDA)-approved for the treatment of acute exacerbations of MS in adults.[1] Controlled clinical trials have shown Acthar Gel 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.

"Suboptimal management of MS relapses may lead to residual deficits, poor recovery and progressive disability.[2,3] In addition, not all patients tolerate or respond effectively to first-line agents such as corticosteroids. As a result, healthcare providers may turn to late-line therapies," said **George Wan,Ph.D., Vice President and Global Head of Health Economics and Outcomes Research at Mallinckrodt.** "This analysis is aimed at addressing the current lack of evidence comparing the cost per response of late-line treatments for MS relapse."

The objective of the analysis was to estimate the cost per response of MS relapse treatment with Acthar Gel versus PMP/IVIg among patients with acute exacerbations of MS (≥1 relapse per year) from a payer perspective. The findings were presented as a poster at the 35thCongress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) and 24th Annual Conference of Rehabilitation in Multiple Sclerosis, held September 11-13, in Stockholm, Sweden. The poster, entitled "Cost Per Response Analysis of Repository Corticotropin Injection Versus Other Late-Line Treatments for Multiple Sclerosis Relapses in Adults," P1059, can be accessed here.

Key Findings

- Although average annual cost of late-line treatments for all patients is similar, the cost per response of Acthar Gel is lower than other late-line treatments.
  - The base case annual cost per response among those treated with Acthar Gel ($141,970) was lower than that with PMP/IVIg ($253,331)
  - Patients who took Acthar Gel had a response rate of 86.6% compared to a response rate of 49.9% among patients who took PMP/IVIg

Methods

- To determine the average annual cost of care, including inpatient, outpatient, and medication costs, patients with MS relapse were identified from the Truven Health Analytics MarketScan® Commercial Claims and Encounters Databases between July 1, 2007 and December 31, 2012.
- Costs were inflated to 2019 USD using the medical consumer price index and data were adjusted for the number of relapses prior to index date, days between exacerbations, comorbid diabetes without complications, year of index exacerbation, and number of outpatient services, hospitalizations, and medications in the six months prior to the index exacerbation.
- Two data sources were used to determine the response rates: Humana Comprehensive Health Insights Database® (January 1, 2008 through July 31, 2015) and the HealthCore Integrated Research Database℠ (January 1, 2006 through

November 30, 2016).

- Response was defined as no additional relapse treatments or procedures within 30 days. Relapse was defined using established claims-based methodology which included an inpatient or outpatient claim with a diagnosis of MS followed by receipt of a relapse treatment or procedure (Acthar Gel, PMP, or IVIg).
- The cost per response compares the annual cost of care per patient achieving MS relapse resolution.
- A one-way deterministic sensitivity analysis was also performed to assess the impact of model inputs on the results for cost per response. The model included certain assumptions
    - The population across the studies were assumed to be homogeneous for the diagnosis of MS.
    - Annual cost of care assumes that patients are treated with intravenous methylprednisolone for the initial relapse and subsequently treated with Acthar Gel or PMP/IVIg for the next relapse.

Limitations

- Relapses were identified based on treatment-seeking behavior across two databases using an established claims-based algorithm; treatment received outside a healthcare visit was not addressed.
- Unrestricted enrollment could underestimate unresolved relapses. PMP and IVIg may be administered as courses of therapy, which would also lead to an underestimation.
- The total annual cost of care did not account for treatment convenience and compliance and the safety profile associated with each therapy.

The analysis was conducted by Mallinckrodt.

About Multiple Sclerosis

MS is a neurologic disorder that affects the central nervous system (i.e., the brain and spinal cord).[4] Symptoms can include fatigue, balance/coordination issues, numbness or tingling, vision problems, muscle spasms, tremors and emotional changes. More than eight in 10 people with MS will experience a relapse, or flare-up, that brings new or worsening symptoms. [5]

Acthar Gel (repository corticotropin injection) Indications

Acthar Gel is an injectable drug approved by the FDA for the treatment of 19 indications. Of these, today the majority of Acthar use is in these indications:

- Adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy)
- Monotherapy for the treatment of infantile spasms in infants and children under 2 years of age
- The treatment of acute exacerbations of multiple sclerosis in adults. Controlled clinical trials have shown Acthar Gel 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
- Treatment during an exacerbation or as maintenance therapy in selected cases of systemic lupus erythematosus
- Inducing a diuresis or a remission of proteinuria in nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus
- Treatment during an exacerbation or as maintenance therapy in selected cases of systemic dermatomyositis (polymyositis)
- The treatment of symptomatic sarcoidosis
- Treatment of 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

IMPORTANT SAFETY INFORMATION

Contraindications

- Acthar should never be administered intravenously
- Administration of live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of Acthar
- Acthar is contraindicated where congenital infections are suspected in infants
- Acthar is contraindicated 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 origins

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-axis (HPA) 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 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. Blood pressure, sodium and potassium levels may need to be monitored
- 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 GI bleeding and gastric ulcer. There is also an increased risk for perforation in patients with certain gastrointestinal disorders. Monitor for signs of bleeding
- Acthar may be associated with central nervous system effects ranging from euphoria, insomnia, irritability, mood swings, personality changes, and severe depression, and 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 activity
- There is 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 for 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

- Common adverse reactions for Acthar are similar to those of corticosteroids and include fluid retention, alteration in glucose tolerance, elevation in blood pressure, behavioral and mood changes, increased appetite and weight gain
- Specific adverse reactions reported in IS clinical trials in infants and children under 2 years of age included: infection, hypertension, irritability, Cushingoid symptoms, constipation, diarrhea, vomiting, pyrexia, weight gain, increased appetite, decreased appetite, nasal congestion, acne, rash, and cardiac hypertrophy. Convulsions were also reported, but these may actually be occurring because some IS patients progress to other forms of seizures and IS sometimes mask other seizures, which 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.

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 expectations regarding its potential impact on patients and anticipated benefits associated with its use. 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.

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[5] National Multiple Sclerosis Society. Relapsing-remitting MS (RRMS). Available at: http://www.nationalmssociety.org/What-is-MS/Types-of-MS/Relapsing-remitting-MS. Accessed September 10, 2019.

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