Mallinckrodt Announces Publication of Human Factors Studies and Arthritis Foundation Ease of Use® Certification of Acthar® Gel (repository corticotropin injection) Single-Dose Pre-filled SelfJect™ Injector

September 17, 2024

– Findings from nine human factors studies, assessing design and user interface, suggest SelfJect functions as an effective delivery device when used as intended[1] –

– The SelfJect delivery device received the Arthritis Foundation's Ease of Use certification –

DUBLIN, Sept. 17, 2024 /PRNewswire/ -- Mallinckrodt plc, a global specialty pharmaceutical company, today announced the publication of findings from seven formative and two validation human factors studies of recently launched Acthar Gel (repository corticotropin injection) Single-Dose Pre-filled SelfJect™ Injector ("SelfJect")[2]. The manuscript, describing the formative and human factor outcomes, was recently published online in *Expert Opinion on Drug Delivery*. Approved by the U.S. Food and Drug Administration (FDA) in February of 2024, SelfJect also received the Arthritis Foundation's Ease of Use® certification. This certification recognizes SelfJect for its easy-to-use design, based on testing by an independent third party.

Acthar Gel is a naturally sourced complex mixture of adrenocorticotropic hormone (ACTH) analogs and other pituitary peptides.[2] Acthar Gel is approved by the FDA for the treatment of several autoimmune disorders and medical conditions known to cause inflammation.[2] SelfJect is available in 40 USP units/0.5 mL and 80 USP units/1.0 mL injectors and must be administered by people 18 years of age or older. SelfJect is not to be used for the treatment of infantile spasms.

Please see Indications and Important Safety Information for Acthar Gel below.

"We're proud of the extensive research and testing conducted to develop SelfJect, including these human factors studies which were critical to our application for FDA approval," said **Lisa French, Executive Vice President & Chief Commercial Officer**. "These results, and the Arthritis Foundation's Ease of Use certification, are a testament to our commitment to modernize Acthar Gel for our patient community. In keeping with our mission of listening for needs, SelfJect provides an administration option designed to better support patients, caregivers, and medical professionals in managing appropriate conditions."

Arthritis Foundation President and CEO Steven Taylor said, "Ease of Use products and packaging are designed to help people with arthritis and those with physical limitations by making everyday tasks easier. We're excited to partner with companies like Mallinckrodt that understand the importance of developing products and packages with the needs of patients at the forefront."

About the Studies

Human factors studies were conducted utilizing SelfJect to assess the design of the injection device and its user interface, as well as mitigate potential use-related hazards, through observation of participants using the device and participant feedback.[1] The published research includes results from nine studies, including seven formative studies, a validation study (with four prior pilot validation studies), and a supplemental validation study with participants including lay users, patients, caregivers, and healthcare providers.[1] The formative studies tested and developed various components such as packaging and instructional material, whereas the validation study evaluated administration of the device with the intended-to-market user interface and representative users in representative simulated-use environments.[1] Four pilot studies then generated additional protocol recommendations for the validation study.[1]

In the 160-participant validation study, 91% (n=146) of participants successfully administered their first injection, with 98% (n=156) cumulative success after the second trial.[1] Use errors were rare with simulated-use (6.9% [n=194] of all evaluated tasks) and knowledge-based (1.6% [n=56] of all evaluated tasks) testing. The most common use errors were related to not appropriately warming the product before administration.[1]

Limitations of the studies include[1]:

- The controlled study setting may not have accurately replicated real-world complexities that play a role in the administration of Acthar Gel via SelfJect, potentially altering the number of study use errors and deviation.
- Injections were performed with placebo gel into an injection pad and not a patient. The feedback that a user receives when

injecting into skin versus a surrogate injection pad may influence use behavior.
- A more realistic delivery container could have been used to cue the participant that this product would arrive cold and would need to be stored appropriately.
- Participant selection bias, reliance on self-reported and qualitative data, and small sample sizes in the formative and pilot studies may have impacted results.

If a customer is interested in learning more about SelfJect, they can reach out to their local representative or visit ActharHCP.com.

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 systemic 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 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 (repository corticotropin injection), the Acthar Gel Single-Dose Pre-filled SelfJect™ Injector, the potential of these products to improve health and treatment outcomes, their potential impact on patients and the availability of Acthar Gel Single-Dose Pre-filled SelfJect Injector in the U.S. in the future. 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; changes in market demand; issues with product quality, manufacturing or supply, or patient safety issues or adverse side effects or adverse reactions associated with Acthar Gel and Acthar Gel Single-Dose Pre-filled SelfJect Injector; and other risks identified and described in more detail in the "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections 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] Linnane A, Lau M, Miranda P, Elliott S. Formative and Validation Human Factors Studies of a New Disposable Prefilled Injection Device for Subcutaneous Delivery of Acthar Gel (Repository Corticotropin Injection). *Expert Opinion on Drug Delivery.* 2024. https://doi.org/10.1080/17425247.2024.2390553.

[2] Acthar® Gel (repository corticotropin injection) [prescribing information]. Bridgewater, NJ: Mallinckrodt ARD LLC.

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