

Mallinckrodt Announces U.S. Food and Drug Administration (FDA) Approves Updated Acthar® Gel (Repository Corticotropin Injection) Label

DUBLIN – March 22, 2021 – [Mallinckrodt plc](#), a global biopharmaceutical company, today announced that the U.S. Food and Drug Administration (FDA) has approved several updates to the full Prescribing Information (PI) for Acthar® Gel (repository corticotropin injection).

The new PI can be accessed [here](#).

The label was updated after the FDA was provided safety monitoring and reporting data spanning more than 60 years. In addition to modernizing the prescribing information, the statement "Common adverse reactions for Acthar Gel are similar to those of corticosteroids" was removed in the prescribing information highlights section of the label; however the warnings and precautions section, which notes potential steroidogenic effects remains largely unchanged. These important updates provide up-to-date safety information available based on a sizable accumulation of pharmacovigilance reporting and clinical trial data, including phase IV clinical studies. The PI was updated in 2019 to characterize Acthar Gel as a naturally sourced complex mixture of adrenocorticotrophic hormone analogs and other pituitary peptides.¹

"We are pleased that the FDA approved these important updates to the Acthar Gel prescribing information to accurately reflect decades of research and clinical experience," said **Steven Romano, M.D., Executive Vice President and Chief Scientific Officer at Mallinckrodt**. "We remain committed to the continued modernization of Acthar Gel, a pharmaceutical product that helps healthcare providers take a multi-targeted approach across multiple indications and patient types, specifically in difficult-to-treat diseases and those patients with recurring and high disease activity."

Since acquiring Acthar Gel in 2014, Mallinckrodt has made a significant investment into the drug. For example, the company built on the existing data through further studies that evaluated the safety and efficacy of Acthar within our indications. Mallinckrodt initiated eight studies targeting combined enrollment of nearly 900 patients, including five randomized controlled clinical trials. In addition, the company has modernized manufacturing, further characterized the mechanism of action and expanded medical affairs and research activities.

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 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. 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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References

¹ Acthar® Gel (repository corticotropin injection) [prescribing information]. Mallinckrodt ARD LLC.