

H.P. Acthar® Gel (repository corticotropin injection) is at the forefront of our ongoing commitment to patients

Serving patients with unmet needs

- ▶ For **Infantile Spasms**, Acthar is indicated as a first-line therapy
- ▶ For patients with other serious medical conditions, Acthar is often prescribed as a later-line treatment when an alternative therapeutic option is needed
- ▶ Acthar is FDA-approved to treat a number of serious, sometimes rare, conditions for which there are very limited or no treatment options available. Some of the approved indications for Acthar include:

Exacerbation of Multiple Sclerosis (MS) in adults

- Acthar is indicated for the treatment of acute exacerbations of MS in adults. Controlled clinical trials have shown Acthar to be effective in speeding the resolution of acute exacerbations of MS. However, there is no evidence that it affects the ultimate outcome or natural history of the disease¹
- MS causes the immune system to attack a person's central nervous system. Some symptoms of an MS relapse may include fatigue, pain, poor balance, and difficulty walking²

Infantile Spasms (IS)

- Acthar is indicated as monotherapy for the treatment of IS in infants and children under 2 years of age¹
- IS is a type of seizure that occurs in infancy and early childhood. Spasms involve sudden, uncontrolled movements³

Proteinuria in Nephrotic Syndrome

- Acthar is indicated to induce a diuresis or a remission of proteinuria in nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus¹
- Proteinuria in nephrotic syndrome occurs when the filters of the kidneys are not working properly. This causes protein to "leak" into a patient's urine and can have varying levels of severity⁴

SELECT IMPORTANT SAFETY INFORMATION

Contraindications

Acthar should never be administered intravenously. The administration of live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses. Acthar is also contraindicated where congenital infections are suspected in infants and 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.

Please see additional **Important Safety Information** on pages 6-7.
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Rheumatoid Arthritis (RA)

- Acthar is indicated as adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in RA, including juvenile RA (selected cases may require low-dose maintenance therapy)¹
- RA is an autoimmune disease that causes the immune system to attack the bones and tissues of the joints. RA can cause pain, stiffness, swelling, and joint damage⁵

Symptomatic Sarcoidosis

- Acthar is indicated for the treatment of symptomatic sarcoidosis¹
- Symptomatic sarcoidosis is an inflammatory disease in which the immune system overreacts, creating granulomas in various parts of the body including the lungs, eyes, heart, liver, and skin⁶

Systemic Dermatomyositis and Polymyositis (DM/PM)

- Acthar is indicated for treatment during an exacerbation or as maintenance therapy in selected cases of systemic DM/PM¹
- DM and PM are inflammatory muscle diseases that cause widespread muscle weakness.^{7,8} Symptoms may include fatigue, muscle tenderness, difficulty swallowing, as well as pain and/or stiffness in joints⁹

Systemic Lupus Erythematosus (SLE)

- Acthar is indicated as treatment during an exacerbation or as maintenance therapy in selected cases of SLE¹
- SLE causes the immune system to attack and destroy healthy tissue, and can produce inflammation of the kidneys, lungs, and heart^{10,11}

Uveitis

- Acthar is indicated for the 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 inflammation¹
- Uveitis is an inflammatory eye condition that affects the uvea, as well as other parts of the eye. Patients may present with pain in the eye, blurred vision, and sensitivity to light¹²

SELECT IMPORTANT SAFETY INFORMATION

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

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Nearly \$400 million invested in Acthar since 2014 as part of our commitment to patients

Our investment in Acthar is building on substantial clinical experience as well as previously completed and largely independent clinical case series and smaller trials; modernizing manufacturing; expanding medical affairs and research activities; and initiating six well-designed, company-sponsored randomized, controlled clinical studies.

Proteinuria Due to Idiopathic Focal Segmental Glomerulosclerosis (FSGS) (PODOCYTE), phase 4

 *236 patients, the largest FSGS study ever undertaken*

Multiple Sclerosis Relapse Registry

 *260 patients*

Multiple Sclerosis Relapse, phase 4

 *66 patients*

Pulmonary Sarcoidosis, phase 4

 *100 patients*

Rheumatoid Arthritis, phase 4

 *232 patients*

Lupus Erythematosus, phase 4

 *162 patients*

SELECT IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd)

- 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

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Collaborative partnership with advocacy groups

At Mallinckrodt, we understand that improving the lives of people with rare disease takes more than medication. It also requires partnering with patient and professional organizations to support education, awareness, and advocacy on behalf of patients. Our goal is to build sustainable relationships that provide value to all stakeholders. That's why we partner with nearly 50 patient/caregiver organizations and professional associations and societies to the benefit of the patients we serve.



Highlights of Our Recent Activities:

- ▶ Worked with over 30 patient/caregiver organizations and 20 professional associations and societies in the areas of rare disease, nephrology, neurology, pulmonology, ophthalmology, and rheumatology
- ▶ Supported over 100 patient education and awareness initiatives that reached thousands of patients and caregivers to offer an opportunity to learn about their disease, increase awareness of appropriate treatment options, and have resources to manage their daily lives
- ▶ Engaged with groups focused on rheumatology, MS, lupus, pulmonology, rheumatoid arthritis, and other disease areas to help inform our pipeline clinical drug development and research activities
- ▶ Collaborated on the development of an infantile spasms tool to help improve early diagnosis and treatment
- ▶ Supported educational events and toolkits to raise awareness of conditions ranging from sarcoidosis to myositis to MS relapse
- ▶ Helped develop an insurance toolkit to help patients with rare diseases navigate the complexities of commercial insurance coverage

These are just a few of the programs we have undertaken in partnership with patient advocacy and professional societies over the past year. In all of our activities, we seek to be a trusted partner, and **we pledge never to use our relationships with patient groups or advocacy organizations to inappropriately market or promote the innovative products we manufacture or sell.**

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When prescribing Acthar, there is an entire support team available through Mallinckrodt

- ▶ Services are available to help patients gain access to and get started on Acthar. The Acthar Hub helps make Acthar available to patients by:
 - Providing individualized Case Manager support to patients and healthcare professionals throughout the insurance approval process
 - Helping patients with valid, on-label prescriptions for Acthar find appropriate financial assistance options, such as:
 - Co-pay assistance for eligible patients with commercial or private insurance
 - Information about Independent Charitable Foundation (ICF) funds for government-insured patients
 - Acthar at no cost through the Acthar Patient Assistance Program for uninsured, underinsured, or rendered uninsured patients*†
- ▶ Offering in-home, online, and phone injection training by licensed nurses at no cost
- ▶ Coordinating home delivery of Acthar with the Specialty Pharmacy

Mallinckrodt's goal continues to be that no appropriate patient goes without access to Acthar on the basis of financial need



Patient and Acthar Coaching Team (ActharPACT)

- ▶ Patient access to personalized support from a registered nurse coach
- ▶ Encouragement and support for patients as they manage their condition
- ▶ Service comes at no cost to patients

Learn more by visiting [Acthar.com](https://acthar.com)



When it comes to drug pricing, we are committed to the following principles:

- ▶ We will price our innovative products responsibly, and in a way that reflects the value they offer patients, providers, and the U.S. healthcare system as a whole
- ▶ If we do increase the list price on any of our innovative drugs or therapies, the total change in a calendar year will not exceed a single digit percentage point

*Acthar Patient Assistance Program patient eligibility criteria:

- Valid Acthar prescription for an FDA-approved indication • Permanent US resident • Household income at or below 700% of the Federal Poverty Level
- Patients may be subject to random income verification to determine eligibility

†Program administered via a third-party organization.

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Warnings and Precautions

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- 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

**Please see Important Safety Information continued on next page.
Please see full Prescribing Information and Medication Guide.**



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IMPORTANT SAFETY INFORMATION (cont'd)

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.

For parents and caregivers of IS patients, please also see Medication Guide.

References: **1.** H.P. Acthar® Gel (repository corticotropin injection) [prescribing information]. Mallinckrodt ARD, Inc. **2.** National Multiple Sclerosis Society. Multiple sclerosis FAQs. <http://www.nationalmssociety.org/What-is-MS/MS-FAQ-s>. Accessed March 13, 2018. **3.** Child Neurology Foundation. Disorder directory: learn from the experts. Infantile spasms. <http://www.childneurologyfoundation.org/disorders/infantile-spasms>. Accessed March 13, 2018. **4.** National Kidney Foundation. Nephrotic syndrome: what you should know. http://www.kidney.org/sites/default/files/01-10-7269_GBG_Nephrotic_Pad3P%281%29.pdf. Accessed March 13, 2018. **5.** Arthritis Foundation. What is Rheumatoid Arthritis? <https://www.arthritis.org/about-arthritis/types/rheumatoid-arthritis/what-is-rheumatoid-arthritis.php>. Accessed March 13, 2018. **6.** Foundation for Sarcoidosis Research. What is sarcoidosis? <http://www.stopsarcoidosis.org/what-is-sarcoidosis>. Accessed March 13, 2018. **7.** Mayo Clinic. Dermatomyositis. <https://www.mayoclinic.org/diseases-conditions/dermatomyositis/symptoms-causes/syc-20353188>. Accessed March 13, 2018. **8.** Mayo Clinic. Polymyositis. <https://www.mayoclinic.org/diseases-conditions/polymyositis/symptoms-causes/syc-20353208>. Accessed March 13, 2018. **9.** Arthritis Foundation. What is Myositis? <https://www.arthritis.org/about-arthritis/types/myositis/>. Accessed March 13, 2018. **10.** Lupus Foundation of America. What is lupus? https://resources.lupus.org/entry/what-is-lupus?utm_source=lupusorg&utm_medium=answersFAQ. Accessed March 13, 2018. **11.** Lupus Foundation of America. How lupus affects the renal (kidney) system. <https://resources.lupus.org/entry/how-lupus-affects-the-renal-system>. Accessed March 13, 2018. **12.** National Eye Institute. Facts about uveitis. <https://nei.nih.gov/health/uveitis/>. Accessed March 9, 2018.



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