FS GS RA ON

Consider Acthar® Gel in patients who have more than one autoimmune or autoinflammatory condition

Patient type:
Tough-to-treat disease

Acthar Gel use in a patient presenting with focal segmental glomerulosclerosis (FSGS), with additional diagnoses of rheumatoid arthritis (RA) and optic neuritis

Patient description: Woman, aged 60, referred by her primary care physician for renal dysfunction

Case study provided by: **Arvind Madan, MD,** Nephrology Associates of Central Florida

This case study is provided for general medical education purposes only and is not a substitute for independent clinical medical judgment. The intent of this case study is to present the experience of an individual patient, which may not represent outcomes in the overall patient population. Response to treatment may vary from patient to patient.

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
- 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
- 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

SELECT 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; 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 origin.

Please see additional Important Safety Information throughout.
Please see accompanying full Prescribing Information or visit ActharHCP.com.

Acthar® GEL
(repository corticotropin injection) 80 U/mL

BEFORE ACTHAR® GEL TREATMENT

History and examination were consistent with tough-to-treat disease[1]

A 60-year-old, white, obese woman was referred by her primary care physician for renal dysfunction. Patient had a renal biopsy 14 years prior that came back normal, a history of intermittent proteinuria, and a previous diagnosis of RA, maintained on prednisone.

FSGS diagnosis

- Proteinuria was 2.5 g at presentation, serum creatinine was at a normal level, and C-reactive protein level was elevated
- A biopsy confirmed the diagnosis of FSGS

History of RA

- Patient was treating her RA with 5 mg of prednisone once daily
- At the time of referral, the patient's joint exam revealed some deformities related to RA but no active synovitis

Patient was treated with an immunosuppressive therapy for her FSGS

Initial treatment decision[1]: The patient was treated with an ACE inhibitor for FSGS and was maintained on 5 mg of prednisone once daily for her RA. Patient's FSGS remained stable for approximately 8 months after initiation of ACE inhibitor treatment.

After 8 months, patient showed signs of FSGS relapse, worsening symptoms, and another disease diagnosis

FSGS

Signs of FSGS relapse
- Serum creatinine concentration was 1.54 mg/dL
- 4+ proteinuria (319 mg/dL)
- Urine protein/creatinine ratio (UPCR) of 9.3 g/g

RA

Patient also experienced painful RA "flares" during ongoing treatment with prednisone

ON

Diagnosis of optic neuritis

- Patient also complained of worsening vision in her right eye and of seeing "water bubbles"
- An exam with an ophthalmologist showed that patient had inflammation and increased redness of the optic nerve
- Patient was diagnosed with optic neuritis

ACE=angiotensin-converting enzyme.

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TREATMENT WITH ACTHAR GEL

When an alternative treatment was needed, her nephrologist turned to Acthar Gel[1]

Patient began treatment with a 6-month regimen of Acthar Gel (40 units twice weekly) in April 2013 for FSGS.

TWICE **WEEKLY**

Dosage should be individualized according to the medical condition of each patient. Frequency and dose of the drug should be determined by considering the severity of the disease and the initial response of the patient.

Sudden withdrawal of Acthar Gel after prolonged use may lead to adrenal insufficiency or recurrent symptoms. It may be necessary to taper the dose and increase the injection interval to gradually discontinue the medication.

Clinically beneficial effects were observed across all 3 conditions after Acthar Gel therapy

FSGS results:

At initial follow-up visit in September 2013, proteinuria and UPCR had **decreased by approximately half** (159 mg/dL and 4.3 g/g, respectively), and serum albumin was 3.4 g/dL.

At a follow-up visit later in September, spot urine UPCR **decreased further** to 1.78 g/g, and serum albumin was 3.7 g/dL. Patient also had grade 2+ bilateral pitting edema.

RA:

Patient experienced fewer RA flares and her pain had decreased by about 50%.

Optic neuritis:

Ophthalmic follow-up showed a decrease in orbital inflammation and reduction in swelling and thickness of the optic nerve in both eyes.

Adverse events

Patient experienced an elevation of her blood pressure and vitreous seeding was observed.

Clinical outcomes may not be solely attributable to Acthar Gel.

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-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

IMPORTANT SAFETY INFORMATION

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- 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 accompanying full Prescribing Information or visit ActharHCP.com for additional Important Safety Information.

Acthar Gel engages melanocortin receptors expressed on immune cells and other tissues throughout the body and is thought to produce both an indirect anti-inflammatory effect and a direct cell modulation effect[2-7]

Melanocortin receptors (MCRs) play a key role in regulating inflammation and other cellular functions. Acthar Gel has been shown *in vitro* to have relative functional potency across all 5 MCRs, with **only 12.5% occurring at MC2R**, which is connected primarily to the production of cortisol.

The exact mechanism of action of Acthar Gel requires further investigation. This information is based on nonclinical and pharmacodynamic data, and the relationship to clinical benefit is unknown.

Acthar Gel was primarily administered in this case to induce the remission of proteinuria in a patient with a history of intermittent proteinuria and a confirmed diagnosis of FSGS. As Dr. Madan noted in his conclusion,

"This case is interesting not only because of its effect in improving proteinuria, but also because it showed clinically beneficial ancillary effects on the patient's inflammatory disease states."

Do you want to learn more about the proposed MOA, or have an appropriate patient who may be a candidate for Acthar Gel?
Talk to your Immunology Sales Specialist today to learn more.

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A 60-year-old woman was referred by her primary care physician for renal dysfunction

- Patient had previously been diagnosed with **RA** and was maintained on **5 mg/day of prednisone**
- **After initial treatment with an ACE inhibitor for FSGS,** patient developed optic neuritis and experienced RA flares
- After treatment with Acthar Gel, **clinical improvement was observed across all three conditions**

SCAN TO LEARN MORE ABOUT ACTHAR GEL CLINICAL EXPERIENCE.

QR Code drives to: https://actharhcp.com/clinical-experience

SELECT IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd)

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References: 1. Madan A. Repository corticotropin injection in a patient presenting with focal segmental glomerulosclerosis, rheumatoid arthritis, and optic neuritis: a case report. *Int Journ Gen Med.* 2015;8:119-124. **2.** Catania A, Lonati C, Sordi A, Carlin A, Leonardi P, Gatti S. The melanocortin system in control of inflammation. *ScientificWorldJournal.* 2010;10:1840-1853. doi:10.1100/tsw.2010.173. **3.** Huang YJ, Galen K, Zweifel B, Brooks LR, Wright AD. Distinct binding and signaling activity of Acthar Gel compared to other melanocortin receptor agonists. *J Recept Signal Transduct Res.* 2021;41(5):425-433. **4.** Olsen NJ, Decker DA, Higgins P, et al. Direct effects of HP Acthar Gel on human B lymphocyte activation in vitro. *Arthritis Res Ther.* 2015;17:300. doi:10.1186/s13075-015-0823-y. **5.** Healy LM, Jang JH, Lin YH, Rao V, Antel JP, Wright D. Melanocortin receptor mediated anti-inflammatory effect of repository corticotropin injection on human monocyte-derived macrophages [ECTRIMS-ACTRIMS abstract EP1481]. *Mult Scler J.* 2017;23(suppl 3):777. **6.** Wright D, Zweifel B, Sharma P, Galen K, Fitch R. Reduced steroidogenic activity of repository corticotropin injection induces a distinct cytokine response following T cell activation in vivo [EULAR abstract AB0082]. *Ann Rheum Dis.* 2019;78(suppl 2):1504. **7.** Benko AL, McAloose CA, Becker PM, et al. Repository corticotrophin injection exerts direct acute effects on human B cell gene expression distinct from the actions of glucocorticoids. *Clin Exp Immunol.* 2018;192(1):68-81.

Mallinckrodt Pharmaceuticals

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