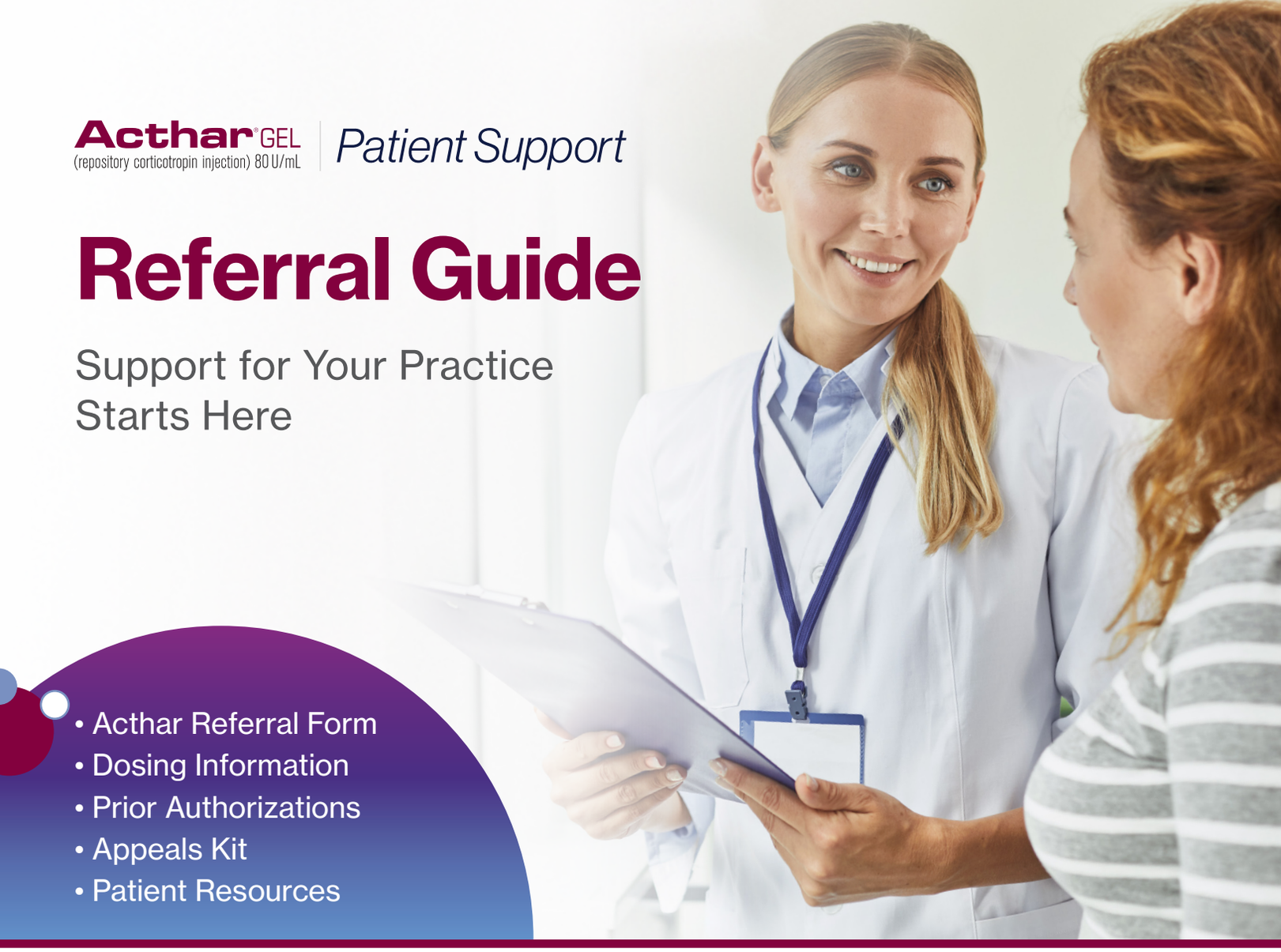
Acthar® GEL
(repository corticotropin injection) 80 U/mL

Patient Support

Referral Guide

Support for Your Practice Starts Here



- Acthar Referral Form
- Dosing Information
- Prior Authorizations
- Appeals Kit
- Patient Resources

INDICATIONS

Acthar® Gel (repository corticotropin injection) is indicated for:

- Treatment during an exacerbation or as maintenance therapy in selected cases of systemic lupus erythematosus
- 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
- 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
- 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
- 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

SELECT IMPORTANT SAFETY INFORMATION

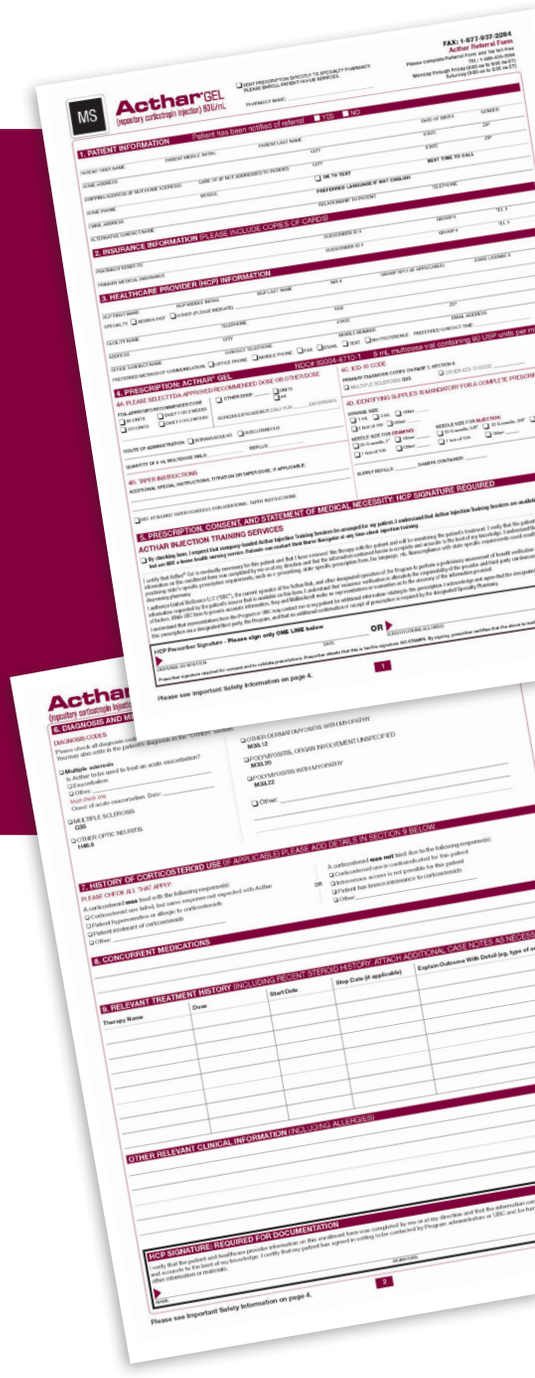
Contraindications

- 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

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

Acthar Referral Form

When writing a prescription for your patient, pay special attention to these key sections of the Referral Form.



No-cost injection training

Initial and date the Acthar Injection Training Services in **section 4** and we'll contact your patient and arrange training to take place in their home, online, or by phone.

Patient Consent for support

To ensure your patient receives our complete level of support during the approval process, have the patient or patient's legal representative sign for Patient Consent in **section 10**.

ICD-10 code list

The backs of the Referral Form pages contain updated **ICD-10 codes**. Make sure you include the same ICD-10 code in **section 4** and **section 6**.

Where, when, and how?

For guidance completing the prescription information in **section 4**, an example Rx for each indication is included in the Dosing Information section of this resource.

Fax completed forms to **1-877-937-2284.**

(Front of pages only. Back pages do not need to be faxed back.)

Please see Important Safety Information throughout and accompanying full Prescribing Information.

Acthar Referral Form (continued)

Prescription Referral Form questions? Contact your Acthar Sales Specialist

Or call **1-888-435-2284** to speak with your Case Manager.
Monday through Friday, 8 AM to 9 PM ET and Saturday, 9 AM to 2 PM ET

With Acthar Patient Support, a dedicated team of experts is ready to help.

Sales Specialists

Your Sales Specialist will be able to answer questions about completing and submitting your Referral Form.

Access and Reimbursement Managers (ARMs)

Your ARM has the experience and knowledge to keep the process moving with local area support.

Nurse Navigators

Once a patient enrolls in Acthar Patient Support, they are assigned a Nurse Navigator who will be their main point of contact as they start and continue their treatment plan.*

Case Managers

Your Case Manager is the main liaison to your practice, providing day-to-day support like scheduling injection training and working with the Specialty Pharmacy.

*Nurse Navigators do not give medical advice and will direct patients to healthcare professionals for any treatment-related questions, including further referrals.

Acthar Referral Forms are included in this guide and are also available at **ActharPatientSupport.com/hcp**

Please see Important Safety Information throughout and accompanying full Prescribing Information.

Dosing Information

Dosage and frequency should be individualized according to the medical condition, severity of disease, and initial response of the patient[1]

- Acthar® Gel (repository corticotropin injection) can be self-administered, which gives patients the flexibility to take it at home or wherever is best for them[1]
- Acthar is a gel when refrigerated. At room temperature it changes to liquid form, ready for injection[1]
- The gel formulation is designed to provide a prolonged release of medication after injection[1]
- Acthar should not be given intravenously. Prolonged use may lead to adrenal insufficiency or recurrent symptoms, which make it difficult to stop treatment. It may be necessary to taper the dose and increase the injection interval to gradually discontinue Acthar[1]
- Acthar should be kept refrigerated (from 36°-46°F or 2°-8°C) between uses[1]

Acthar is provided as a 5-mL multidose vial containing 80 USP units per mL.[1]

Infantile Spasms[1]

Injection: Intramuscular (IM)
Dose: 75 U/m^2 (FDA-approved recommended dosing)
Schedule: Twice daily for 2 weeks with a gradual taper of an additional 2 weeks to avoid adrenal insufficiency

The dose of Acthar is determined using body surface area (BSA).[1] To calculate BSA, use the following formula (Mosteller):

$$BSA(m^2) = \sqrt{\frac{weight\ (kg) \times height\ (cm)}{3600}}$$

To calculate initial dosing, tapered dosing, and vial count, an IS Dosing Calculator is available online at www.actharishcp.com/acthar-dosing-calculator or the iTunes or Google Play app stores.

Acthar should never be administered intravenously.

Multiple Sclerosis Relapse[1]

Injection: Subcutaneous (SC) or intramuscular
Dose: 80-120 units (1-1.5 mL)
Schedule: Daily for 2-3 weeks. May be necessary to taper the dose

Example Rx:
Inject 80 U (1 mL) SC or IM QD for 2 weeks
Quantity of multidose vials: 3
Refills: 1

Nephrology[1]

Injection: Subcutaneous or intramuscular
Dose: 40-80 units (0.5-1 mL)
Schedule: Every 24-72 hours

Example Rx:
Inject 80 U (1 mL) SC or IM every 24-72 hours
Quantity of multidose vials: 5
Refills: 0
Inject 80 U (1 mL) SC BIW for 6 months
Quantity of multidose vials: 2
Refills: 5

Experts have endorsed a dose and duration for Acthar therapy of 80 units twice weekly for 6 months, based on multiple studies.[2] After recognizing that no standardized treatment guidelines exist for managing proteinuria in nephrotic syndrome (NS) due to heterogeneity of diseases/etiologies, a team of leading experts conducted an evidence-based, systematic review to address the need to evaluate all treatments for NS, including the appropriate dosing regimen for Acthar. The review utilized the Delphi Panel Methodology, a scientific research technique that was designed for expert opinions to address important clinical questions.[3,4]

The limitations of the Delphi method include a lack of guidance and agreed-upon standards regarding interpretation and analysis of results. In addition, generalizations are limited and another panel may reach different conclusions.[3]

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

Please see Important Safety Information throughout and accompanying full Prescribing Information.

Dosing Information (continued)

Sarcoidosis[1]

Injection: Subcutaneous or intramuscular
Dose: 40-80 units (0.5-1 mL)
Schedule: Every 24-72 hours

Example Rx:
Inject 80 U (1 mL) SC or IM every 24-72 hours
Quantity of multidose vials: 6
Refills: 5

Rheumatology

	Indication	Source	Injection	Dose	Schedule
Acthar Label Recommended Dosing	**Rheumatic Disorders**	Acthar Prescribing Information[1]	Subcutaneous or intramuscular	40-80 units (0.5-1 mL)	Every 1-3 days
Additional Dosing From Clinical Experience With Acthar	**Dermatomyositis and polymyositis (DM/PM)**	Prospective, open-label proof-of-concept study[5] (N=10)	Subcutaneous	80 units (1 mL)	Twice weekly for 24 weeks
	Systemic lupus erythematosus (SLE)	Prospective, open-label study[6] (N=10)	Subcutaneous	80 units (1 mL)	Once daily for 10 days (optional 5-day extension)
	Psoriatic arthritis (PsA)	Prospective, open-label study[7] (N=15)	Subcutaneous	80 units (1 mL)	Twice weekly for 12-24 weeks
	Rheumatoid arthritis (RA)	Two-part, multicenter, randomized withdrawal study[8] (N=259)	Subcutaneous	80 units (1 mL)	Twice weekly for 12-24 weeks
	Symptomatic sarcoidosis	Retrospective chart review[9] (N=47)	Subcutaneous or intramuscular	40-80 units (0.5-1 mL)	Twice weekly for ≥6 months

Rheumatic Disorders Example Rx:
Inject 40 U (0.5 mL) SC or IM every 24-72 hours
Quantity of multidose vials: 3
Refills: 5

SLE Example Rx:
Inject 80 U (1 mL) SC or daily for 10 days
Quantity of multidose vials: 6
Refills: 5

Ophthalmology[1]

Injection: Subcutaneous or intramuscular
Dose: 40-80 units (0.5-1 mL)
Schedule: Every 24-72 hours

Example Rx:
Inject 80 U (1 mL) SC or IM every 24-72 hours
Quantity of multidose vials: 5
Refills: 0

Select 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

Please see Important Safety Information throughout and accompanying full Prescribing Information.

Prior Authorizations (PAs)

When a PA is required by the health insurance company for Acthar Gel® (repository corticotropin injection), verbal PAs may offer a higher success rate and faster turnaround time than faxed PAs.

Work with your Access and Reimbursement Manager (ARM) and/or Case Manager (CM) to determine the preferred method to submit a PA.

Verbal PA

When available, a verbal PA offers many potential benefits, including:

- Eliminating or reducing paperwork, faxes, and callbacks
- Real-time answers to questions
- Less physician involvement needed down the road
- No scribing errors
- Most importantly, reduced process time, which may allow patients to get on therapy sooner

Faxed/Electronic PA (ePA)

There are a number of portals you may use to submit an electronic PA, such as Sure Scripts® or CoverMyMeds®.

Instructions:

- Fax the Acthar Referral Form to Acthar Patient Support, and make sure your email address is on the form
- If an ePA is available, you will receive an email with a link to the ePA portal and a personal identification number (PIN)
- Click on the link and enter your national provider identifier (NPI) and PIN where indicated
- Once inside the portal, you will be able to electronically complete and submit the prior authorization
- If the submission is not immediately approved, expect to receive approval or denial after only 12 hours

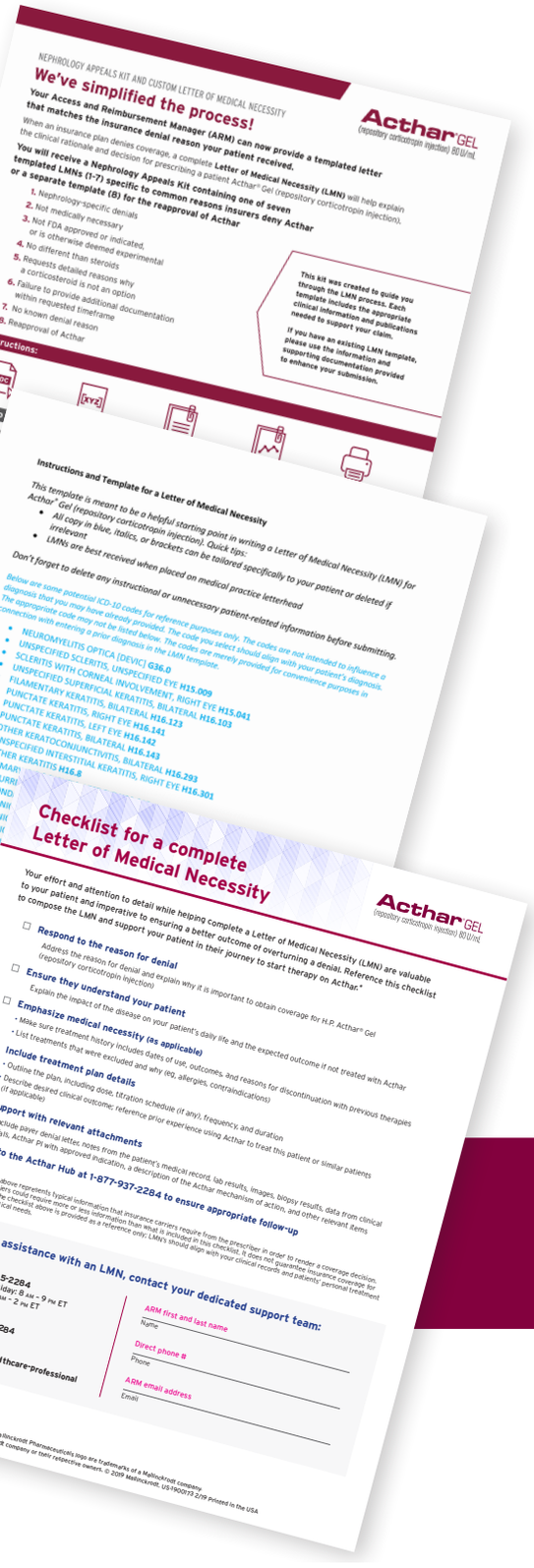
Call **1-888-435-2284** to speak with a Case Manager.

Monday through Friday, 8 AM to 9 PM ET, Saturday, 9 AM to 2 PM ET

Please see Important Safety Information throughout and accompanying full Prescribing Information.

Appeals Kit

When a patient's insurance provider denies coverage for Acthar, the Appeals Kit simplifies the process for you to create and submit a customized Letter of Medical Necessity (LMN).



Appeals Kits are available across all therapeutic areas and include:

Step-by-step instructions

detail how to complete the LMN template.

LMN checklist

lists critical information to include in an effective LMN.

LMN templates

provide sample language for you to customize when addressing an insurance denial.

Supporting resources

are available such as clinical trials, consensus documents, and publications to support why the Acthar prescription may be medically necessary and may be included as part of the response to the health plan's denial.

Acthar Prescribing Information is included as a resource.

Call **1-888-435-2284** to request an Appeals Kit from your ARM.

Please see Important Safety Information throughout and accompanying full Prescribing Information.

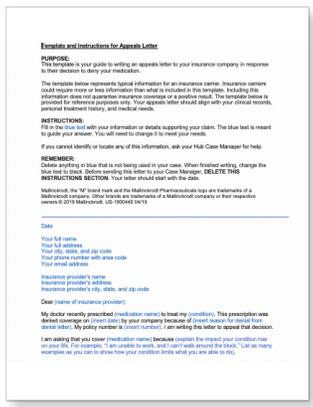
Patient Resources

If an appeal is denied, there are resources available to help patients andtheir caregivers raise their voices, team up with their doctor, and write an appeals letter.

All are available to download at ActtharPatientSupport.com.

Patient Voice Bill of Rights

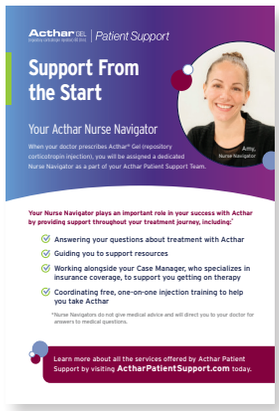
Patient Appeal Discussion Guide



Appeals Letter Template

Additional resources are available to help patients start and continue treatment with Acthar® Gel (repository corticotropin injection). Contact your Case Manager or ARM to order copies for your practice.

Acthar Patient Brochure



Nurse Navigator Leave Behind

ActharPatientSupport.com

From prescription to delivery, Acthar Patient Support is by patients' side every step of the way.

Please see Important Safety Information throughout and accompanying full Prescribing Information.

Assistance Options

Acthar Patient Support works closely with your office throughout the insurance approval process, keeping patients informed along the way. If assistance is needed, the following options may be available:

Commercial or private insurance

If your patients have commercial or private insurance, they may be eligible for the Acthar Commercial Co-pay Program. The program provides the following:

- **$0 co-pay for eligible patients** (see Terms and Conditions below)
- Enrollment over the phone during the Acthar welcome call or anytime they are speaking with their Case Manager
- Automatic processing by the Acthar Specialty Pharmacy with no attempt to collect a co-pay

No insurance coverage

If patients do not have insurance coverage, they may be able to receive assistance options through the Acthar Patient Assistance Program*:

- Mallinckrodt provides Acthar at no cost to eligible patients with a valid, on-label prescription for Acthar who have no insurance, are underinsured, or are rendered uninsured
- Their Case Manager will transfer them to the Acthar Patient Assistance Program to determine eligibility
- This program is administered via a third-party organization

*Acthar Patient Assistance Program 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

Co-Pay Program Terms and Conditions:

- Patient must have a valid Acthar® Gel prescription for an FDA-approved, on-label indication.
- Patient (or patient's legal representative) must be 18 years of age or older to opt into program.
- This program is valid for eligible privately and commercially insured patients.
- This program is not valid for patients covered by Medicare, Medicare D, Medicare Advantage Plans, Medicaid plans (including Medicaid patients enrolled in a qualified health plan purchased through a health insurance exchange [marketplace], TRICARE, Department of Defense (DOD), Veterans Affairs (VA), or any other state or federal medical or pharmacy benefit program.
- The Acthar Commercial Co-pay Program provides drug co-pay assistance of up to $25,000 per calendar year for each eligible patient.
- The program covers out-of-pocket costs for Acthar® Gel only. The program will not and shall not be applied toward the cost of any other product, healthcare provider service, supply charges or other treatment costs.
- This program does not constitute prescription drug coverage or insurance and is not intended to substitute for such coverage. This program is not valid for uninsured patients and cannot be used as primary insurance.
- The offer is not valid for drug costs that are eligible to be reimbursed by private insurance plans or other health or pharmacy benefit programs, which reimburse you for the entire cost of your prescription drugs.
- Enrollment in the co–pay assistance program does not guarantee assistance. Whether an expense is eligible for the copay benefit will be determined at the time the benefit is paid. Eligible co-pay expenses must be in connection with a separately paid claim for Acthar® Gel which is otherwise covered by a private/commercial insurance plan.
- If your insurance status changes, you must notify us prior to fulfilling your next prescription of Acthar® Gel.
- This program offer is limited to 1 membership per person and is not transferable and cannot be combined with any other co-pay assistance program, free trial, discount, prescription savings card, or other offer.
- Patients should consult their insurance provider concerning any limitations that may apply to this program under their insurance policy. Patients are responsible for any co-payment or coinsurance costs above and beyond the program's annual maximum benefit.
- The program is not available where prohibited by law.
- Mallinckrodt reserves the right to rescind, revoke, or amend the co-pay assistance program at any time without notice. Patient will be subject to ineligibility from the Program for violation of these Terms & Conditions.

Please see Important Safety Information throughout and accompanying full Prescribing Information.

Notes

Please see Important Safety Information throughout and accompanying full Prescribing Information.

Select Important Safety Information
Warnings and Precautions (cont'd)

- 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 accompanying full Prescribing Information for additional Important Safety Information.

References: 1. Acthar Gel (repository corticotropin injection) [prescribing information]. Bedminster, NJ: Mallinckrodt ARD LLC. **2.** Bomback AS, Fervenza FC. Membranous nephropathy: approaches to treatment. *Am J Nephrol*. 2018;47(suppl 1):30-42. **3.** Iqbal S, Pipon-Young L. The Delphi method. *Psychologist*. 2009;22(7):598-600. **4.** Tumlin JA, Campbell KN. Proteinuria in nephrotic syndrome: mechanistic and clinical considerations in optimizing management. *Am J Nephrol*. 2018;47(suppl 1):1-2. **5.** Aggarwal R, Marder G, Koontz DC, Nandkumar P, Qi Z, Oddis CV. Efficacy and safety of adrenocorticotropic hormone gel in refractory dermatomyositis and polymyositis. *Ann Rheum Dis*. 2018;77(5):720-727. **6.** Fiechtner JJ, Montroy T. Treatment of moderately to severely active systemic lupus erythematosus with adrenocorticotropic hormone: a single-site, open-label trial. *Lupus*. 2014;23(9):905-912. **7.** Fiechtner JJ, Montroy T, June J. A single-site, investigator initiated open-label trial of H.P. Acthar® Gel (repository corticotropin injection) an adrenocorticotropic hormone (ACTH) analogue in subjects with moderately to severely active psoriatic arthritis (PsA). *J Dermatol Res Ther*. 2016;2(5):1-7. **8.** Fleischmann R, Furst DE, Connolly-Strong E, Liu J, Zhu J, Brasington R. A multicenter study assessing the efficacy and safety of repository corticotropin injection in patients with persistently active rheumatoid arthritis. Poster presented at: European Congress of Rheumatology; June 12-15, 2019; Madrid, Spain. **9.** Baughman RP, Barney JB, O'Hare L, Lower EE. A retrospective pilot study examining the use of Acthar gel in sarcoidosis patients. *Respir Med*. 2016;110:66-72.

Mallinckrodt Pharmaceuticals

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

Patient Support

Acthar® Gel

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use Acthar® Gel safely and effectively. See full prescribing information for Acthar Gel.

Acthar Gel (repository corticotropin injection) INJECTION, GEL for INTRAMUSCULAR | SUBCUTANEOUS use
Initial U.S. Approval: 1952

----------INDICATIONS AND USAGE ----------
- Acthar Gel is indicated as monotherapy for the treatment of infantile spasms in infants and children under 2 years of age. (1.1)
- Acthar Gel is indicated for the treatment of exacerbations of multiple sclerosis in adults. (1.2)
- Acthar Gel may be used for the following disorders and diseases: rheumatic; collagen; dermatologic; allergic states; ophthalmic; respiratory; and edematous state. (1.3 to 1.9)

---------- DOSAGE AND ADMINISTRATION ----------
- In the treatment of infantile spasms, the recommended dose is 150 U/m^2 divided into twice daily intramuscular injections of 75 U/m^2. After 2 weeks of treatment, dosing should be gradually tapered and discontinued over a 2-week period. (2.1)
- In the treatment of acute exacerbations of multiple sclerosis, daily intramuscular or subcutaneous doses of 80-120 units for 2-3 weeks may be administered. It may be necessary to taper the dose. (2.2)
- In the treatment of other disorders and diseases, dosing will need to be individualized depending on the disease under treatment and the medical condition of the patient. It may be necessary to taper the dose. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
- 5 mL multi-dose vial containing 80 USP units per mL. (3)

----------CONTRAINDICATIONS ----------
- Acthar Gel should never be given intravenously.
- Acthar Gel 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, or sensitivity to proteins of porcine origin.
- Administration of live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of Acthar Gel.
- Acthar Gel is contraindicated in children under 2 years of age with suspected congenital infections. (4)
- Treatment of conditions listed within the INDICATIONS AND USAGE section is contraindicated when they are accompanied by primary adrenocortical insufficiency or adrenocortical hyperfunction. (4)

----------WARNINGS AND PRECAUTIONS ----------
- Infections: Increased susceptibility to new infection and increased risk of exacerbation, dissemination or reactivation of latent infections. Signs and symptoms of infection may be masked. (5.1)
- Adrenal Insufficiency after Prolonged Therapy: Monitor for effects of hypothalamic-pituitary-axis suppression after stopping treatment. (5.2)
- Cushing's Syndrome: May occur after prolonged therapy. Monitor for signs and symptoms. (5.2)
- Elevated Blood Pressure, Salt and Water Retention and Hypokalemia: Monitor blood pressure and sodium and potassium levels. (5.3)
- Vaccination: Do not administer live or live attenuated vaccines to patients on immunosuppressive doses. (5.4)
- Masking of Symptoms of Other Underlying Disease/Disorders. Monitor patients for signs of other underlying disease/disorders that may be masked. (5.5)
- Gastrointestinal Perforation and Bleeding: There is a risk for gastric ulcers and bleeding. There is an increased risk of perforation in patients with certain GI disorders. Signs and symptoms may be masked. Monitor for signs of perforation and bleeding. (5.6)
- Behavioral and Mood Disturbances: May include euphoria, insomnia, mood swings, personality changes, severe depression and psychosis. Existing conditions may be aggravated. (5.7)
- Comorbid Diseases: Symptoms of diabetes and myasthenia gravis may be worsened with treatment. (5.8)
- Ophthalmic Effects: Monitor for cataracts, infections and glaucoma. (5.9)
- Immunogenicity Potential: Neutralizing antibodies with chronic administration may lead to a loss of endogenous ACTH activity. (5.10)
- Use in Patients with Hypothyroidism or Liver Cirrhosis: May result in an enhanced effect. (5.11)
- Negative Effects on Growth and Physical Development: Monitor pediatric patients on long term therapy. (5.12)
- Decrease in Bone Density: Monitor for osteoporosis in patients on long term therapy. (5.13)
- Use in Pregnancy: Embryocidal effect. Apprise women of potential harm to the fetus. (5.14)

----------ADVERSE REACTIONS ----------
- Common adverse reactions for Acthar Gel 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. (6)
- Specific adverse reactions resulting from drug use in children under 2 years of age are increased risk of infections, hypertension, irritability, Cushingoid symptoms, cardiac hypertrophy and weight gain. (6.1.1)

To report SUSPECTED ADVERSE REACTIONS, contact Mallinckrodt at 1-800-778-7898 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

---------- DRUG INTERACTIONS----------
- Acthar Gel may accentuate the electrolyte loss associated with diuretic therapy. (7)

----------USE IN SPECIFIC POPULATIONS ----------
- Pregnancy: Acthar Gel 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. (8.1)
- Pediatric Use: Prolonged use of Acthar Gel in children may inhibit skeletal growth. If use is necessary, it should be given intermittently with careful observation. (5.12 and 8.4)

See 17 for Patient Counseling Information and FDA-approved Medication Guide

Revised: 3/2019

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Infantile spasms
Acthar Gel (repository corticotropin injection) is indicated as monotherapy for the treatment of infantile spasms in infants and children under 2 years of age.

1.2 Multiple Sclerosis
Acthar Gel (repository corticotropin injection) is indicated for 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.

1.3 Rheumatic Disorders
As 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.

1.4 Collagen Diseases
During an exacerbation or as maintenance therapy in selected cases of: systemic lupus erythematosus, systemic dermatomyositis (polymyositis).

1.5 Dermatologic Diseases
Severe erythema multiforme, Stevens-Johnson syndrome.

1.6 Allergic States
Serum sickness.

1.7 Ophthalmic Diseases
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.

1.8 Respiratory Diseases
Symptomatic sarcoidosis.

1.9 Edematous State
To induce a diuresis or a remission of proteinuria in the nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus.

2 DOSAGE AND ADMINISTRATION

2.1 Specific Recommended Dosage Regimen for Infantile Spasms in Infants and Children Under 2 Years of Age
In the treatment of infantile spasms, Acthar Gel must be administered intramuscularly. The recommended regimen is a daily dose of 150 U/m^2 (divided into twice daily intramuscular injections of 75 U/m^2) administered over a 2-week period. Dosing with Acthar Gel should then be gradually tapered over a 2-week period to avoid adrenal insufficiency. The following is one suggested tapering schedule: 30 U/m^2 in the morning for 3 days; 15 U/m^2 in the morning for 3 days; 10 U/m^2 in the morning for 3 days; and 10 U/m^2 every other morning for 6-days.

Acthar Gel is typically dosed based on body surface area (BSA). For calculation of body surface area, use the following formula

$$BSA(m^2) = \sqrt{\frac{weight\,(\mathrm{kg}) \times height\,(\mathrm{cm})}{3600}}$$

2.2 Recommended Dosage Regimen for the Treatment of Acute Exacerbations in Adults with Multiple Sclerosis
The recommended dose is daily intramuscular or subcutaneous doses of 80-120 units for 2-3 weeks for acute exacerbations.

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.

Although drug dependence does not occur, sudden withdrawal of Acthar Gel after prolonged use may lead to adrenal insufficiency or recurrent symptoms which make it difficult to stop the treatment. It may be necessary to taper the dose and increase the injection interval to gradually discontinue the medication.

2.3 Recommended Dosage Regimen for Other Indications for Adults and Children Over 2 Years of Age
Dosage should be individualized according to the disease under treatment and the general medical condition of each patient. Frequency and dose of the drug should be determined by considering severity of the disease and the initial response of the patient.

The usual dose of Acthar Gel is 40-80 units given intramuscularly or subcutaneously every 24-72 hours.

Although drug dependence does not occur, sudden withdrawal of Acthar Gel after prolonged use may lead to adrenal insufficiency or recurrent symptoms which make it difficult to stop the treatment. It may be necessary to taper the dose and increase the injection interval to gradually discontinue the medication.

2.4 Preparation
Acthar Gel should be warmed to room temperature before using.

Caution should be taken not to over-pressurize the vial prior to withdrawing the product.

3 DOSAGE FORMS AND STRENGTHS

5 mL multi-dose vial containing 80 USP Units per mL.

4 CONTRAINDICATIONS

Acthar Gel is contraindicated for intravenous administration.

Acthar Gel is contraindicated where congenital infections are suspected in infants.

Administration of live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of Acthar Gel.

Acthar Gel 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 origin.

5 WARNINGS AND PRECAUTIONS

The adverse effects of Acthar Gel are related primarily to its steroidogenic effects. Not all of the adverse events described below have been seen after treatment with Acthar Gel, but might be expected to occur *[see Adverse Reactions (6.3)]*.

5.1 Infections
Acthar Gel may increase the risks related to infections with any pathogen, including viral, bacterial, fungal, protozoan or helminthic infections. Patients with latent tuberculosis or tuberculin reactivity should be observed closely, and if therapy is prolonged, chemoprophylaxis should be instituted.

5.2 Cushing's Syndrome and Adrenal Insufficiency Upon Withdrawal
Treatment with Acthar Gel can cause hypothalamic-pituitary-axis (HPA) suppression and Cushing's syndrome. These conditions should be monitored especially with chronic use.

Suppression of the HPA may occur following prolonged therapy with the potential for adrenal insufficiency after withdrawal of the medication. Patients should be monitored for signs of insufficiency such as weakness, hyperpigmentation, weight loss, hypotension and abdominal pain.

The symptoms of adrenal insufficiency in infants treated for infantile spasms can be difficult to identify. The symptoms are non-specific and may include anorexia, fatigue, lethargy, weakness, excessive weight loss, hypotension and abdominal pain. It is critical that parents and caregivers be made aware of the possibility of adrenal insufficiency when discontinuing Acthar Gel and should be instructed to observe for, and be able to recognize, these symptoms *[see Patient Counseling Information (17)]*.

The recovery of the adrenal gland may take from days to months so patients should be protected from the stress (e.g. trauma or surgery) by the use of corticosteroids during the period of stress.

The adrenal insufficiency may be minimized in adults and infants by tapering of the dose when discontinuing treatment.

Signs or symptoms of Cushing's syndrome may occur during therapy but generally resolve after therapy is stopped. Patients should be monitored for these signs and symptoms such as deposition of adipose tissue in characteristics sites (e.g., moon face, truncal obesity), cutaneous striae, easy bruisability, decreased bone mineralization, weight gain, muscle weakness, hyperglycemia, and hypertension.

5.3 Elevated Blood Pressure, Salt and Water Retention and Hypokalemia
Acthar Gel can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium and calcium. Dietary salt restriction and potassium supplementation may be necessary. Caution should be used in the treatment of patients with hypertension, congestive heart failure, or renal insufficiency.

5.4 Vaccination
Administration of live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of Acthar Gel. Killed or inactivated vaccines may be administered; however, the response to such vaccines can not be predicted. Other immunization procedures should be undertaken with caution in patients who are receiving Acthar Gel, especially when high doses are administered, because of the possible hazards of neurological complications and lack of antibody response.

5.5 Masking Symptoms of Other Diseases
Acthar Gel often acts by masking symptoms of other diseases/disorders without altering the course of the other disease/disorder. Patients should be monitored carefully during and for a period following discontinuation of therapy for signs of infection, abnormal cardiac function, hypertension, hyperglycemia, change in body weight and fecal blood loss.

5.6 Gastrointestinal Perforation and Bleeding
Acthar Gel can cause GI bleeding and gastric ulcer. There is also an increased risk for perforation in patients with certain gastrointestinal disorders. Signs of gastrointestinal perforation, such as peritoneal irritation, may be masked by the therapy. Use caution where there is the possibility of impending perforation, abscess or other pyogenic infections, diverticulitis, fresh intestinal anastomoses, and active or latent peptic ulcer.

5.7 Behavioral and Mood Disturbances
Use of Acthar Gel may be associated with central nervous system effects ranging from euphoria, insomnia, irritability (especially in infants), mood swings, personality changes, and severe depression, to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated.

5.8 Comorbid Diseases
Patients with a comorbid disease may have that disease worsened. Caution should be used when prescribing Acthar Gel in patients with diabetes and myasthenia gravis.

5.9 Ophthalmic Effects
Prolonged use of Acthar Gel may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves and may enhance the establishment of secondary ocular infections due to fungi and viruses.

5.10 Immunogenicity Potential
Acthar Gel is immunogenic. Limited available data suggest that a patient may develop antibodies to Acthar Gel after chronic administration and loss of endogenous ACTH and Acthar Gel activity. Prolonged administration of Acthar Gel may increase the risk of hypersensitivity reactions. Sensitivity to porcine protein should be considered before starting therapy and during the course of treatment should symptoms arise.

5.11 Use in Patients with Hypothyroidism or Liver Cirrhosis
There is an enhanced effect in patients with hypothyroidism and in those with cirrhosis of the liver.

5.12 Negative Effects on Growth and Physical Development
Long-term use of Acthar Gel may have negative effects on growth and physical development in children. Changes in appetite are seen with Acthar Gel therapy, with the effects becoming more frequent as the dose or treatment period increases. These effects are reversible once Acthar Gel therapy is stopped. Growth and physical development of pediatric patients on prolonged therapy should be carefully monitored.

5.13 Decrease in Bone Density
Decrease in bone formation and an increase in bone resorption both through an effect on calcium regulation (i.e. decreasing absorption and increasing excretion) and inhibition of osteoblast function may occur. These, together with a decrease in the protein matrix of the bone (secondary to an increase in protein catabolism) and reduced sex hormone production, may lead to inhibition of bone growth in children and adolescents and to the development of osteoporosis at any age. Special consideration should be given to patients at increased risk of osteoporosis (i.e., postmenopausal women) before initiating therapy, and bone density should be monitored in patients on long term therapy.

5.14 Use in Pregnancy
Acthar Gel has been shown to have an embryocidal effect. Apprise women of potential harm to the fetus *[see Use in Specific Populations (8.1)]*.

6 ADVERSE REACTIONS

Please refer to *Adverse Reactions in Infants and Children Under 2 Years of Age (Section 6.1.1)* for consideration when treating patients with Infantile Spasms. The adverse reactions presented in Section 6.2 are primarily provided for consideration in use in adults and in children over 2 years of age, but these adverse reactions should also be considered when treating infants and children under 2 years of age.

Acthar Gel causes the release of endogenous cortisol from the adrenal gland. Therefore all the adverse effects known to occur with elevated cortisol may occur with Acthar Gel administration as well. Common adverse reactions include fluid retention, alteration in glucose tolerance, elevation in blood pressure, behavioral and mood changes, increased appetite and weight gain.

6.1 Clinical Studies Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug, and may not reflect the rates observed in practice.

6.1.1 Adverse Reactions in Infants and Children Under 2 Years of Age
While the types of adverse reactions seen in infants and children under age 2 treated for infantile spasms are similar to those seen in older patients, their frequency and severity may be different due to the very young age of the infant, the underlying disorder, the duration of therapy and the dosage regimen. Below is a summary of adverse reactions specifically tabulated from source data derived from retrospective chart reviews and clinical trials in children under 2 years of age treated for infantile spasms. The number of patients in controlled trials at the recommended dose was too few to provide meaningful incidence rates or to permit a meaningful comparison to the control groups.

TABLE: Incidence (%) of Treatment Emergent Adverse Events Occurring in ≥ 2% of Acthar Gel (repository corticotropin injection) Infants and Children under 2 years of Age

System Organ Class	Recommended 75 U/m² bid n=122, (%)	150 U/m² qd n=37 (%)
Cardiac disorders		
Cardiac Hypertrophy	3	0
Endocrine disorders		
Cushingoid	3	22
Gastrointestinal disorders		
Constipation	0	5
Diarrhea	3	14
Vomiting	3	5
General disorders and administration site conditions		
Irritability	7	19
Pyrexia	5	8
Infections and infestations		
Infection*	20	46
Investigations		
Weight gain	1	3
Metabolism and nutrition disorders		
Increased appetite	0	5
Decreased appetite	3	3
Nervous system disorders		
Convulsion†	12	3
Respiratory, thoracic and mediastinal disorders		
Nasal Congestion	1	5
Skin and subcutaneous tissue disorders		
Acne	0	14
Rash	0	8
Vascular disorders		
Hypertension	11	19

* Specific infections that occurred at ≥ 2% were candidiasis, otitis media, pneumonia and upper respiratory tract infections. † In the treatment of Infantile Spasms, other types of seizures/convulsions may occur because some patients with infantile spasms progress to other forms of seizures (for example, Lennox-Gastaut Syndrome). Additionally, the spasms sometimes mask other seizures and once the spasms resolve after treatment, the other seizures may become visible.

These adverse reactions may also be seen in adults and children over 2 years of age when treated for other purposes and with different doses and regimens.

6.2 Postmarketing Experience
The following adverse reactions associated with the use of Acthar Gel have been identified from postmarketing experience with Acthar Gel. Only adverse events that are not listed above as adverse events reported from retrospective chart reviews and non-sponsor conducted clinical trials and those not discussed elsewhere in labeling, are listed in this section. Because the adverse reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency or establish a causal relationship to use with Acthar Gel. Events are categorized by system organ class. Unless otherwise noted these adverse events have been reported in infants, children and adults.

6.2.1 Allergic Reactions
Allergic responses have presented as dizziness, nausea and shock (adults only).

6.2.2 Cardiovascular
Necrotizing angitis (adults only) and congestive heart failure.

6.2.3 Dermatologic
Skin thinning (adults only), facial erythema and increased sweating (adults only).

6.2.4 Endocrine
Decreased carbohydrate tolerance (infants only) and hirsutism.

6.2.5 Gastrointestinal
Pancreatitis (adults only), abdominal distention and ulcerative esophagitis.

6.2.6 General Disorders and Administration Site Conditions
Injection site reactions.

6.2.7 Metabolic
Hypokalemic alkalosis (infants only).

6.2.8 Musculoskeletal
Muscle weakness and vertebral compression fractures (infants only).

6.2.9 Neurological
Headache (adults only), vertigo (adults only), subdural hematoma, intracranial hemorrhage (adults only), and reversible brain shrinkage (usually secondary to hypertension) (infants only).

6.3 Possible Additional Steroidogenic Effects
Based on steroidogenic effects of Acthar Gel certain adverse events may be expected due to the pharmacological effects of corticosteroids. The adverse events that may occur but have not been reported for Acthar Gel are:

6.3.1 Dermatologic
Impaired wound healing, abscess, petechiae and ecchymoses, and suppression of skin test reactions.

6.3.2 Endocrine
Menstrual irregularities.

6.3.3 Metabolic
Negative nitrogen balance due to protein catabolism.

6.3.4 Musculoskeletal
Loss of muscle mass and aseptic necrosis of femoral and humeral heads.

6.3.5 Neurological
Increased intracranial pressure with papilledema, (pseudo-tumor cerebri) usually after treatment, and subdural effusion.

6.3.6 Ophthalmic
Exophthalmos.

7 DRUG INTERACTIONS

Formal drug-drug interaction studies have not been performed.

Acthar Gel may accentuate the electrolyte loss associated with diuretic therapy.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Pregnancy Class C: Acthar Gel has been shown to have an embryocidal effect. There are no adequate and well-controlled studies in pregnant women. Acthar Gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Acthar Gel, when treating a nursing mother, a decision should be made whether to discontinue nursing or to discontinue the drug, considering the risk and benefit to the mother.

8.4 Pediatric Use

Acthar Gel is indicated as monotherapy for the treatment of infantile spasms in infants and children less than 2 years of age. Both serious and other adverse reactions in this population are discussed in Warnings and Adverse Reactions in Infants and Children Under 2 Years of Age *[see Sections 5 and 6.1.1]*.

The efficacy of Acthar Gel for the treatment of infantile spasms in infants and children less than 2 years of age was evaluated in a randomized, single blinded (video EEG interpreter blinded) clinical trial and an additional active control supportive trial *[see Clinical Studies (14)]*. A responding patient was defined as having both complete cessation of spasms and elimination of hypsarrhythmia.

Safety in the pediatric population for infantile spasms was evaluated by retrospective chart reviews and data from non-sponsor conducted clinical trials *[see Adverse Reactions (6.1.1)]*. While the types of adverse reactions seen in infants and children under 2 years of age treated for infantile spasms are similar to those seen in older patients, their frequency and severity may be different due to the very young age of the infant, the underlying disorder, the duration of therapy and the dosage regimen. Effects on growth are of particular concern *[see Warnings and Precautions (5.12)]*. Serious adverse reactions observed in adults may also occur in children *[see Warnings and Precautions (5)]*.

10 OVERDOSAGE

While chronic exposure to Acthar Gel at high doses can be associated with a variety of potential serious adverse effects, it is not expected that a single high dose, or even several large doses, has the potential for serious adverse effects compared to a standard dose. There have been no reports of death or acute overdose symptoms from Acthar Gel in clinical studies or in the published literature.

The intramuscular route of administration makes it unlikely that an inadvertent acute overdose will occur. The typical daily dose of Acthar Gel to treat an infant that has a BSA of 0.4 m^2 would be 60 U/day. Using the 1-cc syringe supplied with Acthar Gel, the maximum amount that can be injected is 80 U/injection, which is a well-tolerated single dose.

11 DESCRIPTION

Acthar Gel is a naturally sourced complex mixture of adrenocorticotropic hormone analogs and other pituitary peptides. The Acthar Gel manufacturing process converts the initial porcine pituitary extract with low ACTH content into a mixture having modified porcine ACTH and other related peptide analogs solubilized in gelatin. A major component in the formulated complex mixture is N-25 deamidated porcine ACTH (1-39).

Acthar Gel is supplied as a sterile preparation in 16% gelatin to provide a prolonged release after intramuscular or subcutaneous injection. Acthar Gel also contains 0.5% phenol, not more than 0.1% cysteine (added), sodium hydroxide and/or acetic acid to adjust pH and water for injection.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The mechanism of action of Acthar Gel in the treatment of infantile spasms is unknown.

Acthar Gel and endogenous ACTH stimulate the adrenal cortex to secrete cortisol, corticosterone, aldosterone, and a number of weakly androgenic substances. Prolonged administration of large doses of Acthar Gel induces hyperplasia and hypertrophy of the adrenal cortex and continuous high output of cortisol, corticosterone and weak androgens. The release of endogenous ACTH is under the influence of the nervous system via the regulatory hormone released from the hypothalamus and by a negative corticosteroid feedback mechanism. Elevated plasma cortisol suppresses ACTH release.

Acthar Gel is also reported to bind to melanocortin receptors.

The trophic effects of endogenous ACTH and Acthar Gel on the adrenal cortex are not well understood beyond the fact that they appear to be mediated by cyclic AMP.

ACTH rapidly disappears from the circulation following its intravenous administration; in people, the plasma half-life is about 15 minutes. The pharmacokinetics of Acthar Gel have not been adequately characterized.

The maximal effects of a trophic hormone on a target organ are achieved when optimal amounts of hormone are acting continuously. Thus, a fixed dose of Acthar Gel will demonstrate a linear increase in adrenocortical secretion with increasing duration for the infusion.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Adequate and well-controlled studies have not been done in animals. Human use has not been associated with an increase in malignant disease *[see Warnings and Precautions (5.14) and Use in Specific Populations (8.1)]*.

14 CLINICAL STUDIES

The effectiveness of Acthar Gel as a treatment for infantile spasms was demonstrated in a single blinded (video EEG interpreter blinded) clinical trial in which patients were randomized to receive either a 2 week course of treatment with Acthar Gel (75 U/m^2 intramuscular twice daily) or prednisone (1 mg/kg by mouth twice daily). The primary outcome was a comparison of the number of patients in each group who were treatment responders, defined as a patient having complete suppression of both clinical spasms and hypsarrhythmia on a full sleep cycle video EEG performed 2 weeks following treatment initiation, rated by an investigator blinded to treatment. Thirteen of 15 patients (86.7%) responded to Acthar Gel as compared to 4 of 14 patients (28.6%) given prednisone ($p<0.002$). The 2-week treatment was followed by a 2-week period of taper. Nonresponders to the prednisone treatment were eligible to receive Acthar Gel treatment. Seven of 8 patients (87.5%) responded to Acthar Gel after not responding to prednisone. Similarly, the 2 nonresponder patients from the Acthar Gel treatment were eligible to receive treatment with prednisone. One of the 2 patients (50%) responded to the prednisone treatment after not responding to Acthar Gel.

A supportive single-blind, randomized clinical trial comparing high-dose, long-duration treatment (150 U/m^2 once daily for 3 weeks, n=30) of Acthar Gel with low-dose, short-duration treatment (20 U once daily for 2 weeks, n=29) for the treatment of infantile spasms was also evaluated in infants and children less than 2 years of age. Nonresponders (defined as in the previously described study) in the low-dose group received a dose escalation at 2 weeks to 30 U once daily. Nominal statistical superiority of the high dose treatment, as compared to the low dose treatment, was observed for cessation of spasms but not for the resolution of hypsarrhythmia.

16 HOW SUPPLIED / STORAGE AND HANDLING

Acthar Gel (repository corticotropin injection) is supplied as 5 mL multi-dose vial (63004-8710-1) containing 80 USP Units per mL. Acthar Gel (repository corticotropin injection) should be warmed to room temperature before using. Do not over pressurize the vial prior to withdrawing the product.

Store Acthar Gel (repository corticotropin injection) under refrigeration between 2° to 8°C (36° to 46°F). Product is stable for the period indicated on the label when stored under the conditions described.

17 PATIENT COUNSELING INFORMATION

Caretakers of patients with infantile spasms should be informed of the availability of a Medication Guide, and they should be instructed to read the Medication Guide prior to administering Acthar Gel. Patients should be instructed to take Acthar Gel only as prescribed. They should not stop treatment suddenly unless instructed by their physician to do so.

Patients, their caregivers and families should be advised as to the importance of the need for careful monitoring while on and during titration from Acthar Gel treatment and the importance of not missing scheduled doctor's appointments.

Patients, their caregivers and families should be advised that if the patient develops an infection or fever they should contact their physician. They should be educated that a fever may not necessarily be present during infection. The patient should also try to limit contact with other people with infections to minimize the risk of infection while taking Acthar Gel *[see Warnings and Precautions (5.1) and Adverse Reactions (6.1.1)]*.

Patients, their caregivers and families should be advised that if the patient experiences an increase in blood pressure they should contact their physician *[see Warnings and Precautions (5.3) and Adverse Reactions (6.1.1)]*.

Patients, their caregivers and families should be advised that if the patient or the caregiver notices blood or a change in color of the patient's stool they should contact their physician *[see Warnings and Precautions (5.6)]*.

Caregivers and families of infants and children treated with Acthar Gel should be informed that the patient may show signs of irritability and sleep disturbances. These effects are reversible once Acthar Gel therapy is stopped *[see Warnings and Precautions (5.7) and Adverse Reactions (6.1.1)]*.

Patients, their caregivers and families should be advised that changes in appetite, most often leading to weight gain, are seen with Acthar Gel therapy, becoming more frequent as the dose or treatment period increases. These effects are reversible once Acthar Gel therapy is stopped *[see Warnings and Precautions (5.12) and Adverse Reactions (6.1.1)]*.

Patients, their caregivers and families should be advised that the patient may be monitored for signs of adrenal insufficiency such as weakness, fatigue, lethargy, anorexia, weight loss, hypotension, abdominal pain or hyperpigmentation (adults only) after treatment has stopped. Since the recovery of the adrenal gland varies from days to months, patients may need to be protected from the stress of trauma or surgery by the use of corticosteroids during the period of stress *[see Warnings and Precautions (5.2)]*.

Patients should be advised not to be vaccinated with live or live attenuated vaccines during treatment with Acthar Gel. Additionally, other immunization procedures in patients or in family members who will be in contact with the patient should be undertaken with caution while the patient is taking Acthar Gel *[see Warnings and Precautions (5.4)]*.

Patients, their caregivers and families should be advised that prolonged use of Acthar Gel in children may result in Cushing's syndrome and associated adverse reactions, may inhibit skeletal growth, and may cause osteoporosis and decreased bone density. If prolonged use is necessary, Acthar Gel should be given intermittently along with careful observation *[see Warnings and Precautions (5.2), (5.12), and (5.13) and Adverse Reactions (6.1.1)]*.

Patients, their caregivers and families should be informed that Acthar Gel may mask symptoms of other diseases/disorders without altering the course of the other disease/disorder. The patient will need to be monitored carefully during and for a period following discontinuation of therapy for signs of infection, abnormal cardiac function, hypertension, hyperglycemia, change in body weight, and fecal blood loss *[see Warnings and Precautions (5.5)]*.

In the treatment of Infantile Spasms, other types of seizures may occur because some patients with infantile spasms progress to other forms of seizures (for example, Lennox-Gastaut Syndrome). Additionally the spasms sometimes mask other seizures and once the spasms resolve after treatment with Acthar Gel, the other seizures may become visible. Parents and caregivers should inform their physician of any new onset of seizures so that appropriate management can then be instituted *[see Adverse Reactions (6.1.1)]*.

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