Corticotropin Medical Drug Criteria Program Summary

POLICY REVIEW CYCLE

Effective Date
04-07-2025

Date of Origin

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Acthar® Gel (repository corticotropin) Intramuscular injection Subcutaneous injection	Infantile Spasm (IS) in infants and children under 2 years of age NOTE: Acthar is FDA approved for numerous indications, however, the FDA has only evaluated clinical trials in infants under 2 years of age with infantile spasms(7,8) Indicated in the following disorders: • Acute exacerbations of multiple sclerosis (MS) 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 • 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 • Collagen diseases: during an exacerbation or as maintenance therapy in selected cases of systemic lupus erythematosus and systemic dermatomyositis (polymyositis) • Dermatologic diseases: severe erythema multiforme and Stevens-Johnson syndrome • Allergic states: serum sickness • 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, and anterior segment inflammation • Respiratory diseases: Symptomatic sarcoidosis • Edematous states: 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		1
Purified Cortrophin® Gel (repository corticotropin) Multiple-dose vial for intramuscular	Indicated in the following disorders: • 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, acute gouty arthritis		6

Agent(s)	FDA Indication(s)	Notes	Ref#
or subcutaneous injection Single-dose prefilled syringe for subcutaneous injection only	• Collagen diseases: during an exacerbation or as maintenance therapy in selected cases of systemic lupus erythematosus and systemic dermatomyositis (polymyositis) • Dermatologic diseases: severe erythema multiforme (Stevens-Johnson syndrome) and severe psoriasis • Allergic states: atopic dermatitis and serum sickness • Ophthalmic diseases: severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as allergic conjunctivitis, keratitis, iritis and iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, and anterior segment inflammation • Respiratory diseases: Symptomatic sarcoidosis • Edematous states: 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 • Nervous system: Acute exacerbations of multiple sclerosis		

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Infantile Spasms	Infantile spasm (IS), also referred to as West Syndrome, is a specific seizure syndrome that is characterized by clinical flexor or extensor spasms, often involving the extremities and head/neck; developmental regression (intellectual disability); and electroencephalography (EEG) finding of hypsarrhythmia (chaotic brain waves).(2,3) Neurological and/or developmental outcomes in patients with IS are usually poor. Children with symptomatic spasms more frequently exhibit neurological deficits and cognitive and developmental delays, while a higher percentage of patients with idiopathic/cryptogenic IS may have a normal or near-normal outcome if appropriate treatment is initiated in a timely fashion. Goals of therapy for IS includes complete cessation of clinical events and resolution of hypsarrhythmia or modified hypsarrhythmia on video EEG.(3) Guidelines recommend ACTH and vigabatrin for the treatment of infantile spasms. Both ACTH and vigabatrin may be useful for short-term treatment, but ACTH is preferred over vigabatrin, except in patients with tuberous sclerosis. Hormonal therapy (ACTH or prednisolone) has been shown to lead to better neurodevelopmental outcomes in patients with cryptogenic IS when compared to vigabatrin.(2,3) Guidelines recommend treating for 14 days and then tapering down, as response is typically seen within 14 days or sooner. Low dose ACTH is probably as effective as high-dose ACTH therapy and should be considered as an alternative to high dose therapy.(2) A 2010 U.S. consensus statement suggests initiating a taper of ACTH after two weeks of therapy at the maximum dose. No data is available to guide therapy in relapse in patients who responded to an initial treatment course. Typically, a second course (four to six weeks) of the agent that was previously effective in obtaining control is administered.(4) Acthar Gel was first approved in 1952 prior to the 1962 drug amendments requiring clinical trials proving safety and efficacy.(1,5) Repository corticotropin injection is available as Acthar Gel (Mallinckrodt Pharmaceuticals, Inc), formerly known as H.P. Acthar Gel (Questcor Pharmaceuticals), and Purified Cortrophin Gel (ANI Pharmaceuticals, Inc). Acthar Gel and Purified Cortrophin Gel are highly purified sterile preparations of the adrenocorticotropic hormone (ACTH) available in 16% gelatin (for Acthar Gel) or 15% gelatin (for Purified Cortrophin Gel) to provide a prolonged release after intramuscular or subcutaneous injection.(9)

	Repository corticotropin injection was originally approved by the U.S. Food and Drug Administration (FDA) in 1952 for a broad range of corticosteroid-responsive conditions including rheumatic, collagen, dermatologic, allergic states, ophthalmic, respiratory and edematous states. Current labeled indications include multiple sclerosis, rheumatic disorders, collagen diseases, dermatologic diseases, allergic states, ophthalmologic diseases, respiratory diseases, and edematous states. In addition, the FDA approved the use of repository corticotropin injection (Acthar Gel only) for treatment of infantile spasms in infants and children under 2 years of age.(9) In August 2021, the U.S. FDA approved Purified Cortrophin Gel for virtually the same indications as Acthar Gel except for the infantile spasms indication. There are a lack of clinical studies comparing the effectiveness of ACTH gel to corticosteroids in corticosteroid-responsive conditions. In addition, there is no reliable evidence of the effectiveness of ACTH gel in persons who have failed to respond to corticosteroids.(9)
Efficacy	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. Non-responders 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 non-responder 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.(1) 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. Non-responders (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.(1) There is no clinical data for the FDA indication for Cortrophin Gel. No additional clinical trials for Cortrophin were completed to show efficacy for the approved indications.(6)
Safety	Acthar Gel is contraindicated in the following:(1) • Intravenous administration • Suspicion of congenital infections in infants under 2 years of age • 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 or hyperfunction, or sensitivity to porcine proteins • Concomitant administration of live or live attenuated vaccines in patients receiving immunosuppressive doses of Acthar Gel Purified Cortrophin gel is contraindicated in the following:(6) • Intravenous administration • 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 or hyperfunction, or sensitivity to porcine proteins

REFERENCES

Number	Reference
1	Acthar Gel prescribing information. Mallinckrodt ARD, Inc. February 2024.
2	Go, CY, Mackay MT, Weiss SK, Weiss SK, et al. Evidence-based guideline update: Medical treatment of infantile spasms: American Academy of Neurology. Neurology 2012;78;1974-1980
3	Nelson, Gary Rex. Management of Infantile Spasms. Transl Pedatr . 2015;4(4):260-270.
4	Pellock JM, Hrachovy R, Shinnar S, et al. Infantile spasms: a U.S. consensus report. Epilepsia 2010; 51:2175.
5	White Junod, S. (2008). FDA and Clinical Drug Trials: A Short History. Washington. https://www.fda.gov/media/110437/download.
6	Purified Cortrophin Gel prescribing information. ANI Pharmaceuticals, Inc. October 2023.
7	U.S. Food and Drug Administration. Center for Drug Evaluation and Research. (2010). Application 022432Orig1s000 Internal Consult on draft labeling (Package Insert) for H.P. Acthar Gel. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2010/022432Orig1s000OtherR.pdf
8	U.S. Food and Drug Administration. Center for Drug Evaluation and Research. (2010). Application 022432Orig1s000 Action Memo for NDA 22-432, for the use of H.P. Acthar Gel (repository corticotrophin injection) in the treatment of Infantile Spasms (IS). https://www.accessdata.fda.gov/drugsatfda_docs/nda/2010/022432Orig1s0900SumR.pdf
9	U.S. Food and Drug Administration. Center for Drug Evaluation and Research. (2022). Application: 008975Orig1s008. Approval Package for Purified Cortrophin Gel. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2022/008975Orig1s008.pdf.

POLICY AGENT SUMMARY – MEDICAL PRIOR AUTHORIZATION

HCPC Codes	Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
J0801	Acthar	corticotropin inj gel	80 UNIT/ML	M ; N ; O ; Y	N		
	Acthar gel	corticotropin subcutaneous gel auto-injector	40 UNIT/0.5ML ; 80 UNIT/ML	M ; N ; O ; Y	N		
J0802	Cortrophin	corticotropin inj gel	80 UNIT/ML	M ; N ; O ; Y	N		
J0802	Purified cortrophin	corticotropin subcutaneous gel prefilled syr ; corticotropin subcutaneous gel prefilled syringe	40 UNIT/0.5ML ; 80 UNIT/ML	M ; N ; O ; Y	N		

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Acthar	corticotropin inj gel	80 UNIT/ML	Commercial ; HIM ; ResultsRx
Acthar gel	corticotropin subcutaneous gel auto-injector	40 UNIT/0.5ML ; 80 UNIT/ML	Commercial ; HIM ; ResultsRx
Cortrophin	corticotropin inj gel	80 UNIT/ML	Commercial ; HIM ; ResultsRx
Purified cortrophin	corticotropin subcutaneous gel prefilled syr ; corticotropin subcutaneous gel prefilled syringe	40 UNIT/0.5ML ; 80 UNIT/ML	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
PA	

Preferred Target Agent(s)	Non-Preferred Target Agent(s)
Acthar Gel (repository corticotropin)	Purified Cortrophin Gel (repository corticotropin)

Target Agent(s) will be approved when ALL of the following are met:

1. The patient has a diagnosis of infantile spasms AND
2. The patient is less than 24 months of age AND
3. If the client has preferred agent(s), then ONE of the following:
   A. The requested agent is a preferred agent OR
   B. The patient has tried and had an inadequate response to the preferred agent(s) OR
   C. The patient has an intolerance or hypersensitivity to the preferred agent(s) that is NOT expected to occur with the requested agent OR
   D. The patient has and FDA labeled contraindication to the preferred agent(s) that is NOT expected to occur with the requested agent AND
4. The patient does NOT have any FDA labeled contraindications to the requested agent AND
5. The requested quantity (dose) is within FDA labeled dosing for the requested indication

Length of Approval: 6 months

Target Agent(s) will NOT be approved and are NOT medically necessary for all other indications including but not limited to:

1. Multiple Sclerosis
2. Rheumatic Disorders
3. Collagen diseases
4. Dermatologic diseases
5. Allergic states
6. Ophthalmic diseases
7. Respiratory diseases
8. Edematous states

The effectiveness of repository corticotropin has not been demonstrated as clinically superior to conventional corticosteroids and/or immunosuppressive therapy for uses other than infantile spasms.