H.P. Acthar Gel® (repository corticotropin) Prior Authorization Criteria Program Summary

This criteria applies to Commercial, NetResults A series, NetResults F series, and Health Insurance Marketplace.

OBJECTIVE
The intent of the H.P. Acthar Gel (repository corticotropin) Prior Authorization (PA) Criteria is to appropriately select patients for therapy according to product labeling and/or clinical studies and to verify appropriate FDA labeled dosing for specified indications. The PA criteria will direct its use to the clinically supported indication of infantile spasms. Criteria require that patients do not have any FDA labeled contraindications to use H.P. Acthar Gel.

TARGET DRUGS
H.P. Acthar Gel® (repository corticotropin)

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
H.P. Acthar Gel will be approved when ALL of the following are met:

1. The patient does not have any FDA labeled contraindication(s) to therapy with the requested agent
   AND
2. BOTH of the following:
   a. The patient has been diagnosed with Infantile spasms
      AND
   b. The patient is < 24 months of age
   AND
3. The dose is within the FDA labeled dosing for the requested indication.

Approved Indication	Dosing
Infantile Spasm	**Treatment:** 150 U/m^2 IM in divided doses daily for 14 days **Taper:** 30 U/m^2 in the a.m. for 3 days; 15 U/m^2 in the a.m. for 3 days; 10 U/m^2 in the a.m. for 3 days; and 10 U/m^2 every other a.m. for 6 days

U- units; IM- intramuscularly

Length of Approval: 6 months

Agent	Contraindication(s)
H.P. Acthar gel	intravenous administration, scleroderma, osteoporosis, systemic fungal infection, ocular herpes simplex, recent surgery, a history or presence of a peptic ulcer, congestive heart failure, uncontrolled hypertension, or sensitivity to proteins of

	porcine origin, administration of live or live attenuated vaccines, children < 2 years of age with suspected congenital infections, treatment of FDA approved indications when accompanied by primary adrenocortical insufficiency or hyperfunction

FDA APPROVED INDICATIONS AND DOSAGE[1]

FDA Approved Indications	Dosing
Infantile Spasm	**Treatment:** 150 U/m^2 IM in divided doses daily for 14 days **Taper:** 30 U/m^2 in the a.m. for 3 days; 15 U/m^2 in the a.m. for 3 days; 10 U/m^2 in the a.m. for 3 days; and 10 U/m^2 every other a.m. for 6 days.
Acute exacerbation of Multiple Sclerosis	80-120 units IM or SC daily for 2-3 weeks
Rheumatic Disorders: Adjunctive for short-term administration	
Psoriatic arthritis	Usual dose is 40-80 units IM or SC every 24-72 hours. Dosing should be individualized. Tapering may be necessary for discontinuation.
Rheumatoid arthritis	
Juvenile rheumatoid arthritis	
Ankylosing spondylitis	
Collagen Diseases	
Systemic lupus erythematosus	Usual dose is 40-80 units IM or SC every 24-72 hours. Dosing should be individualized. Tapering may be necessary for discontinuation.
Systemic dermatomyositis (polymyositis)	
Dermatologic Diseases	
Severe erythema multiforme	Usual dose is 40-80 units IM or SC every 24-72 hours. Dosing should be individualized. Tapering may be necessary for discontinuation.
Steven-Johnson syndrome	
Allergic States	
Serum sickness	Usual dose is 40-80 units IM or SC every 24-72 hours. Dosing should be individualized. Tapering may be necessary for discontinuation.
Ophthalmic Diseases	
Keratitis	Usual dose is 40-80 units IM or SC every 24-72 hours. Dosing should be individualized. Tapering may be necessary for discontinuation.
Iritis	
Iridocyclitis	
Diffuse posterior uveitis and choroiditis	
Optic neuritis	
Chorioretinitis	
Anterior segment inflammation	
Respiratory Diseases	
Symptomatic Sarcoidosis	Usual dose is 40-80 units IM or SC every 24-72 hours. Dosing should be individualized. Tapering may be necessary for discontinuation.
Edematous State	
Induce a diuresis or a remission of proteinuria in the nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus.	Usual dose is 40-80 units IM or SC every 24-72 hours. Dosing should be individualized. Tapering may be necessary for discontinuation.

U- units; IM- intramuscularly; SC- subcutaneously

CLINICAL RATIONALE
H.P. Acthar Gel (repository corticotropin) is an adrenocorticotropin hormone (ACTH). H.P. Acthar Gel along with endogenous ACTH stimulates the adrenal cortex to secrete cortisol, corticosterone, and aldosterone. H.P. Acthar Gel was approved by the FDA in 1952. Clinical efficacy and safety data for the majority of indications, with the exception of infantile spasm is lacking. According to the manufacturer little data is available for the general indications of rheumatic, collagen, dermatologic, allergic states, ophthalmic, respiratory, edematous disorders/diseases, and multiple sclerosis and these indications were grandfathered in by the FDA. Based on the lack of both efficacy and safety data for the above referenced grandfathered indications, these additional disorders will be considered unsupported indications.

Infantile Spasm (West Syndrome)
Infantile spasm (IS) is a specific seizure type seen in an epilepsy syndrome of infancy. It is characterized by spasms, developmental regression and a specific pattern of electroencephalography (EEG) testing called hypsarrhythmia (chaotic brain waves). Onset typically occurs between 4 and 8 months of age and usually stops by age five. More than half of the children with IS will develop other types of seizures. There seems to be a correlation between IS and Lennox-Gastaut Syndrome, an epileptic disorder of later childhood.[9]

The efficacy of corticotropin was evaluated in a single blinded trial with patients randomized to either a 2 week course of corticotropin (75 U/m^2 intramuscular twice daily) or prednisone (1 mg/kg orally 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. Thirteen of 15 patients (86.7%) responded to corticotropin as compared to 4 of 14 (28.6%) given prednisone ($p<0.002$). Nonresponders to prednisone were eligible for corticotropin treatment. Seven of 8 patients (87.5%) responded to corticotropin after prednisone failure. Similarly, patients not responding to corticotropin were eligible for prednisone. One of 2 patients (50%) responded to prednisone after failure of corticotropin.[1]

The National Institute for Health and Care Excellence (NICE) guidelines (2012) recommend vigabatrin or prednisolone as first line therapy for infantile spasm (West's syndrome).[2]

The American Academy of Neurology (AAN) guidelines (2012) determined low dose ACTH should be considered for treatment of infantile spasms. Both ACTH and vigabatrin may be useful for short-term treatment but ACTH is preferred over vigabatrin. ACTH or prednisolone may be considered for use in preference to vigabatrin in patients with cryptogenic infantile spasms, to potentially improve development outcomes. There is insufficient evidence that other forms of corticosteroids are as effective in the treatment of infantile spasms as ACTH for short-term treatment. Low dose ACTH is probably as effective as high-dose therapy. There is insufficient evidence to show that other agents and combination therapy are effective in short-term treatment of infantile spasms.[3] A US consensus report acknowledges that data is lacking on the best approach to take if spasms recur following an initial clinical response to treatment. The report suggests options including returning to the previously effective treatment agent (at maximum dose) or implementing a new therapy.[10]

Safety
Administration with H.P. Acthar Gel is contraindicated for intravenous administration, suspicion of congenital infections in children < 2, 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. Administration of live or live attenuated vaccines is also contraindicated. The adverse events associated with H.P. Acthar Gel are primarily related to its steroidogenic effects.[1]

REFERENCES

1. H.P. Acthar Gel Prescribing Information. Mallinckrodt. January 2015.
2. NICE Guidelines. The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care. 2012. Available at: http://publications.nice.org.uk/the-epilepsies-the-diagnosis-and-management-of-the-epilepsies-in-adults-and-children-in-primary-and-cg137/appendix-e-pharmacological-treatment. Accessed on 8/22/13.
3. 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.
4. Deleted
5. Deleted
6. Deleted
7. Deleted
8. Deleted
9. NINDS Infantile Spasms Information Page. Available at: http://www.ninds.nih.gov/disorders/infantilespasms/infantilespasms.htm. Accessed 11/11/11.
10. Pellock et al. Infantile spasms: A U.S. consensus report. *Epilepsia* 2010;10:2175-2189.