Clinical Policy: Corticotropin (H.P. Acthar)

Reference Number: ERX.SPA.72
Effective Date: 10.01.16
Last Review Date: 02.18 Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Corticotropin (H.P. Acthar®) is an adrenocorticotropic hormone analogue.

FDA Approved Indication(s)
H.P. Acthar is indicated:
- For the treatment of infantile spasms in infants and children under 2 years of age as monotherapy
- For the treatment of exacerbations of multiple sclerosis (MS) in adults

H.P. Acthar Gel may also be used for the following disorders and diseases: rheumatic, collagen, dermatologic, allergic states, ophthalmic, respiratory, and edematous state.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that H.P. Acthar is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. West Syndrome (Infantile Spasms) (must meet all)**:**
1. Diagnosis of West syndrome (infantile spasms);
2. Prescribed by or in consultation with a neurologist;
3. Age < 2 years;
4. Dose does not exceed 150 U/m^2 per day (divided into twice daily IM injections of 75 U/m^2).

Approval duration: 3 months

B. Multiple Sclerosis (must meet all)**:**
1. Diagnosis of MS;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Prescribed for acute exacerbations of MS;
5. Failure of a recent (within the last 30 days) trial of at least 7 day course of corticosteroid therapy for acute exacerbations of MS, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 120 units per day.

Approval duration: 1 months

C. Nephrotic Syndrome (must meet all)**:**
a. Diagnosis of nephrotic syndrome and associated (a or b):
   a. Systemic lupus erythematosus;
   b. Idiopathic nephropathy/glomerulonephritis;
b. Prescribed by or in consultation with a nephrologist;
c. Age > 2 years;
d. Failure of oral steroids, unless contraindicated or clinically significant adverse effects are experienced;
e. Failure of ≥ 2 of the following agents: tacrolimus, cyclosporine, mycophenolate, rituximab, unless contraindicated or clinically significant adverse effects are experienced;
f. Dose does not exceed 80 units given intramuscularly or subcutaneously every 24 hours.

Approval duration: 3 months

B. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. West Syndrome (Infantile Spasms) (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Age is < 2 years old;
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed 150 U/m^2 per day (divided into twice daily injections of 75 U/m^2).

Approval duration: 3 months (West syndrome – one renewal limit)

B. Multiple Sclerosis: HP Acthar is not indicated for continuous use for this indication. Reauthorization requests must be reviewed against the initial approval criteria.

C. Nephrotic Syndrome (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Prescribed by or in consultation with a nephrologist;
3. Documentation of positive response to therapy;
4. Dose does not exceed 80 units given intramuscularly or subcutaneously every 24 hours.

Approval duration: 3 months

D. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 3 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
ACTH: adrenocorticotropic hormone
MS: multiple sclerosis

Appendix B: Therapeutic Alternatives
Not applicable.

Appendix C: General Information
- Common adverse reactions for H.P. 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.
- The initial approval of H.P. ACTH gel occurred prior to the Kefauver-Harris amendment to the Federal Food, Drug and Cosmetic Act of 1962, which introduced the requirement of "substantial evidence" of two adequate and well controlled trials. At the time of the original approval drug manufacturers only had to show the drug was safe for use in humans. The original data included

case reports from a few physicians describing patients with conditions originally treated with Acthar powder that were transferred to treatment with Acthar Gel and gave dosing guidance for treatment of these individual conditions.

- The efficacy H.P. Acthar Gel in the following conditions has not been proven in well-designed clinical trials and its use is considered experimental, They are also not FDA approved indications:
  - 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; systemic dermatomyositis (polymyositis)
  - Dermatologic Diseases: severe erythema multiforme, 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; anterior segment inflammation
  - Respiratory Diseases: symptomatic sarcoidosis
  - 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
- For acute exacerbations in multiple sclerosis, the results of trials that analyzed direct comparisons have shown no significant differences between ACTH and methylprednisolone (MP) in both rate and degree of recovery after exacerbation. Indirect comparisons suggest a significantly greater effect of MP versus ACTH, with MP conferring greater benefit compared with ACTH (odds ratio (OR) 0.20, 95% CI 0.09 to 0.45 vs OR 0.46, 95% CI 0.28 to 0.77).
- Studies evaluating the use of ACTH in acute exacerbations of multiple sclerosis ranged from 14 to 21 days in length and evaluated one course of therapy. To date, retreatment with ACTH has not been evaluated in clinical trials.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
West syndrome (infantile spasms)	150 U/m^2 IM divided into twice daily injections of 75 U/m^2 administered over a 2-week period. After 2 weeks, H.P. Acthar should be gradually tapered over a 2-week period	150 U/m^2/day
Acute exacerbation of MS	80-120 units IM or SC daily for 2-3 weeks	120 units/day
Nephrotic syndrome	80 units IM or SC every 24 hours	80 units/day

VI. Product Availability

Multi-dose vial: 5 mL containing 80 USP units per mL

VII. References

1. H.P. Acthar Prescribing Information. Hazelwood, MO: Mallinckrodt ARD, Inc.; January 2015. Available at http://www.acthar.com. Accessed November 13, 2017.
2. Go CY, Mackay MT, Weiss SK, et al. Evidenced-based guideline update: Medical treatment of infantile spasms: Report of the guideline development subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology. June 12, 2012; 78(24): 1974-80. Reaffirmed July 18, 2015.
3. Pellock JM, Hrachovy R, Shinnar S, et al. Infantile spasms: A U.S. consensus report. Epilepsia. October 2010; 51(10): 2175-89.
4. Berkovich R, Agius M. Mechanisms of action of ACTH in the management of relapsing forms of multiple sclerosis. Ther Adv Neurol Disord. March 2014; 7(2): 83–96.
5. Filippini G, Brusaferri F, Sibley WA, et al. Corticosteroids or ACTH for acute exacerbations in multiple sclerosis. Cochrane Database Syst Rev. 2000; (4): CD001331.

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12. Madan A, Mijovic-Das S, Stankovic A, et al. Acthar gel in the treatment of nephrotic syndrome: A multicenter retrospective case series. BMC Nephrol. March 31, 2016; 17:37.
13. Thompson AJ, Kennard C, Swash M, Summers B, Yuill GM, Shepherd DI, et al. Relative efficacy of intravenous methylprednisolone and ACTH in the treatment of acute relapse in MS. Neurology 1989; 39(7): 969–71.
14. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2016. Available at: http://www.clinicalpharmacology-ip.com/.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from USS.CP.PHAR.56 H.P. Acthar and Sabril and converted to new template. Removed all requests for documentation and safety criteria. Removed labeled indications and criteria that do not have clinical studies showing effectiveness and superiority over corticosteroid therapy. Retained criteria for infantile spasms and MS. Infantile spasms: modified approval duration to 4 weeks. MS: added age/dosing and modified approval duration to max 3 weeks based on PI; added criteria for failure or contraindication of oral corticosteroids for MS; added requirement for adherent use of disease modifying therapy.	07.16	09.16
- Converted to new template. - Added Nephrotic syndrome and other indications criteria. - Updated references.	07.01.17	08.17
1Q18 annual review: - Removed indications not supported by well-designed clinical trials as noted in *Appendix C*; retained indication due for nephrotic syndrome in policy due to appeal overturn report - West syndrome – removed EEG requirement to confirm diagnosis; added neurologist prescriber requirement. - MS – added requirement for 7 day course of corticosteroid therapy for acute exacerbations; approval duration reduced to one month for initial as this medication is not indicated to used chronically and for continued approval for MS was referred to the initial criteria. - References reviewed and updated.	02.06.17	02.18

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.