

## **Clinical Policy: Repository Corticotropin Injection (H.P. Acthar Gel)**

Reference Number: CP.PHAR.168

Effective Date: 03.01.16

Last Review Date: 02.18

Line of Business: Commercial, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### **Description**

Repository Corticotropin Injection (H.P. Acthar<sup>®</sup> Gel) is adrenocorticotrophic hormone in 16% gelatin.

### **FDA Approved Indication(s)**

H.P. Acthar Gel is indicated:

- For the treatment of infantile spasms in infants and children under 2 years of age as monotherapy
- For the treatment of acute exacerbations of multiple sclerosis (MS) in adults.

### **Policy/Criteria**

*Provider must submit documentation (including such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> that H.P. Acthar Gel 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<sup>2</sup> per day (divided into twice daily injections of 75 U/m<sup>2</sup>).

**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):

1. Diagnosis of nephrotic syndrome and associated (a or b):
  - a. Systemic lupus erythematosus;
  - b. Idiopathic nephropathy/glomerulonephritis;
2. Age > 2 years;
3. Prescribed by or in consultation with a nephrologist;
4. Failure of oral steroids, unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of  $\geq 2$  of the following agents: tacrolimus, cyclosporine, mycophenolate, rituximab, unless contraindicated or clinically significant adverse effects are experienced;
6. Prescribed daily dose does not exceed 80 units given intramuscularly or subcutaneously every 24 hours.

**Approval duration: 3 months**

**D. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

**A. West Syndrome (Infantile Spasms)** (must meet all):

1. Currently receiving medication via Centene benefit 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  $150 \text{ U/m}^2$  per day (divided into twice daily injections of  $75 \text{ U/m}^2$ );

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

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

**C. Nephrotic Syndrome** (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Prescribed by or in consultation with a nephrologist;
3. Documentation of positive response to therapy;
4. Prescribed daily 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 Centene benefit and documentation supports positive response to therapy.

- Approval duration: Duration of request or 3 months (whichever is less);** or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

**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 policies – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

ACTH: adrenocorticotrophic 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 HP Acthar Gel has 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 <sup>2</sup> IM divided into twice daily injections of 75 U/m <sup>2</sup> administered over a 2-week period. After 2 weeks, H.P. Acthar Gel should be gradually tapered over a 2-week period.	150 U/m <sup>2</sup> per day (divided into twice daily intramuscular injections of 75 U/m <sup>2</sup> )
Acute exacerbation of MS	80-120 units IM/SC daily for 2-3 weeks	120 units IM/SC per 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 <https://www.acthar.com/pdf/Acthar-PI.pdf>. 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, Brusaferrri F, Sibley WA, et al. Corticosteroids or ACTH for acute exacerbations in multiple sclerosis. *Cochrane Database Syst Rev*. 2000; (4): CD001331.
6. Berkovich R, Bakshi R, Amezcua L, et al. Adrenocorticotrophic hormone versus methylprednisolone added to interferon B in patients with multiple sclerosis experiencing breakthrough disease: A randomized, rater-blinded trial. *Ther Adv Neurol Disord*. January 2017; 10(1): 3-17.

7. Beck L, Bomback AS, Choi M, et al. KDOQI commentary on the 2012 KDIGO clinical practice guidelines for glomerulonephritis. *Am J Kidney Dis.* 2013; 62(3): 403-441.
8. Lieberman KV and Pavlova-Wolf A. Adrenocorticotrophic hormone therapy for the treatment of idiopathic nephrotic syndrome in children and young adults: A systematic review of early clinical studies with contemporary relevance. *J Nephrol.* 2017; 30: 35-44.
9. Hladunewich MA, Cattran D, Beck LH, et al. A pilot study to determine the dose and effectiveness of adrenocorticotrophic hormone (H.P. Acthar® Gel) in nephrotic syndrome due to idiopathic membranous nephropathy. *Nephrol Dial Transplant.* 2014; 29: 1570-1577.
10. Hogan J, Bomback AS, Mehta K, et al. Treatment of idiopathic FSGS with adrenocorticotrophic hormone gel. *Clin J Am Soc Nephrol.* December 6, 2013; 8(12): 2072-2081.
11. Chen Y, Schieppati A, Cai G, et al. Immunosuppression for membranous nephropathy: A systematic review and meta-analysis of 36 clinical trials. *Clin J Am Soc Nephrol.* May 7, 2013; 8(5): 787-796.
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 CP.PHAR.56.H.P. Acthar and Sabril. Criteria: added contraindications; updated MS approval period 2 to 3 weeks with a week for taper if necessary; updated infantile spasm approval period to 4 weeks; updated definition of nephrotic syndrome for children and adults; included all FDA labeled indications and criteria for each. Background: limited to Description/MOA and FDA approved indications. Appendices: added abbreviation key; removed the following appendices - contraindications, tentative treatment plan, examples of side effects - and included pertinent information from appendices directly into criteria.	02.16	03.16
Added criteria for failure of oral corticosteroids for MS. Added criteria for rheumatic diseases, collagen disorders, ophthalmic diseases, and “other indications.”	03.16	03.16
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.	05.16	05.16

Reviews, Revisions, and Approvals	Date	P&T Approval Date
<p>For MS, added requirement for adherent use of disease modifying therapy and contraindications to both oral and injectable glucocorticoids Modified approval duration for acute MS exacerbation to max 3 weeks based on PI.</p>		
<p>Safety information removed. Infantile spasms approval duration is increased from 4 weeks to 3 months and continuing approval x 1 is added. MS approval duration is increased from 4 weeks to 3 months. Continued approval is per Medical Director review. Nephrotic syndrome criteria are added for recalcitrant cases. Other PI indications are added for recalcitrant cases with the qualification that requests be supplemented by peer-reviewed literature. Continued approval is per Medical Director review. References updated.</p>	05.17	05.17
<p>1Q18 annual review: - Combined Medicaid and commercial policies. - Removed indications not supported by well-designed clinical trials as noted in <i>Appendix C</i>; 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- 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.</p>	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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

©2016 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene<sup>®</sup> and Centene Corporation<sup>®</sup> are registered trademarks exclusively owned by Centene Corporation.