

## Clinical Policy: Corticotropin (H.P. Acthar, Purified Cortrophin Gel)

Reference Number: ERX.SPA.72

Effective Date: 10.01.16

Last Review Date: 02.22

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® Gel, Purified Cortrophin™ Gel) is adrenocorticotrophic hormone (ACTH) in 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

H.P. Acthar Gel and Purified Cortrophin Gel are indicated for the treatment of acute exacerbations of multiple sclerosis (MS) in adults

### Policy/Criteria

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

*Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.*

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that H.P. Acthar and Purified Cortrophin Gel are **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. Request is for H.P. Acthar Gel;
3. Diagnosis is confirmed by electroencephalogram (EEG);
4. Prescribed by or in consultation with a neurologist;
5. Age < 2 years;
6. Dose does not exceed 150 U/m<sup>2</sup> per day (divided into twice daily IM 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. Member has been adherent to disease modifying therapy for MS (e.g., Aubagio®, Avonex®, Betaseron®, Copaxone®, Gilenya®, Plegridy®, Rebif®);
7. For H.P. Acthar Gel requests, member must use Purified Cortrophin Gel, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. Dose does not exceed 120 units (1.5 mL) per day and 6 vials total (see Appendix D).

**Approval duration: 3 weeks**

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

1. Diagnosis of nephrotic syndrome associated with one of the following (a - f):
  - a. Idiopathic membranous nephropathy (IMN);
  - b. Focal segmental glomerulosclerosis;
  - c. Minimal change disease (MCD);
  - d. Membranoproliferative glomerulonephritis;
  - e. Lupus nephritis;
  - f. IgA nephropathy;
2. Prescribed by or in consultation with a nephrologist;
3. Age > 2 years;
4. Failure of oral corticosteroid therapy, unless contraindicated or clinically significant adverse effects are experienced;
5. For IMN and MCD: Failure of cyclophosphamide, unless contraindicated or clinically significant adverse effects are experienced;
6. Failure of two of the following, unless clinically significant adverse effects are experienced or all are contraindicated: tacrolimus, cyclosporine, mycophenolate, rituximab;
7. For H.P. Acthar Gel requests, member must use Purified Cortrophin Gel, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. Dose does not exceed 80 units (1 mL) per day.

**Approval duration: 3 months**

**D. 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. Request is for H.P. Acthar Gel;
3. Age < 2 years;
4. Member is responding positively to therapy;
5. If request is for a dose increase, new 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 (one renewal limit)**

**B. Multiple Sclerosis**

1. Re-authorization is not permitted. H.P. Acthar Gel and Purified Cortrophin Gel are not indicated for continuous use for this indication. Members must meet the initial approval criteria.

**Approval duration: Not applicable**

**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. Member is responding positively to therapy;
3. For H.P. Acthar Gel requests, member must use Purified Cortrophin Gel, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, new dose does not exceed 80 units (1 mL) per day.

**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;
- B.** The following conditions have not been proven in well-designed clinical trials and use is considered experimental:
  1. 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;
  2. Collagen diseases: During an exacerbation or as maintenance therapy in selected cases of: systemic lupus erythematosus; systemic dermatomyositis (polymyositis);
  3. Dermatologic diseases: severe erythema multiforme, Stevens-Johnson syndrome;
  4. Allergic states: serum sickness;
  5. 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;
  6. Respiratory diseases: symptomatic sarcoidosis.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

ACTH: adrenocorticotrophic hormone  
EEG: electroencephalogram  
FDA: Food and Drug Administration

IMN: idiopathic membranous nephropathy  
MCD: minimal change disease  
MS: multiple sclerosis

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
tacrolimus (Prograf <sup>®</sup> )	Nephrotic syndrome: 0.05-0.075 mg/kg/day PO in two divided doses 12 hours apart	0.075 mg/kg/day
cyclosporine (Neoral <sup>®</sup> , Sandimmune <sup>®</sup> )	Nephrotic syndrome: 3.5-5 mg/kg/day PO in two equally divided doses 12 hours apart	5 mg/kg/day
cyclophosphamide	Nephrotic syndrome: 20 mg/kg/day PO for a 6-month course with alternating monthly cycles of PO and IV corticosteroids	20 mg/kg/day
mycophenolate (CellCept <sup>®</sup> )	Nephrotic syndrome: 2-3 g/day PO	3 g/day
Rituxan <sup>®</sup> (rituximab)	Nephrotic syndrome: 375 mg/m <sup>2</sup> IV every week	375 mg/m <sup>2</sup> /week
methylprednisolone (Medrol <sup>®</sup> , Solu-Medrol <sup>®</sup> )	Acute exacerbation of multiple sclerosis: IM: 160 mg IM daily for 1 week, followed by 64 mg every other day for 1 month Oral: 160 mg PO per day for 1 week, followed by 64 mg every other day for 1 month	160 mg/day
prednisone (Deltasone <sup>®</sup> )	Acute exacerbation of multiple sclerosis: 200 mg/day PO for 1 week, followed by 80 mg PO every other day for 1 month	200 mg/day
dexamethasone (Decadron <sup>®</sup> )	Acute exacerbation of multiple sclerosis: 30 mg PO QD for 1 week followed by 4 to 12 mg PO every other day for 1 month	30 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Intravenous administration
  - 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
  - Treatment of FDA approved indications accompanied by primary adrenocortical insufficiency or adrenocortical hyperfunction
  - H.P. Acthar Gel only:
    - Administration of live or live attenuated vaccines in patients receiving immunosuppressive doses of H.P Acthar Gel
    - Children under 2 years of age with suspected congenital infections
- Boxed warning(s): none reported

*Appendix D: 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. Acthar 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
- Although H.P. Acthar Gel use in nephrotic syndrome has not been evaluated in well-designed clinical trials, it would be appropriate to allow use after exhausting alternative treatment options with higher quality of evidence to support their use that are supported by the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines for glomerulonephritis (e.g., corticosteroids, cyclophosphamide, cyclosporine, tacrolimus, mycophenolate, Rituxan).
- 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 3 to 21 days in length and evaluated a reducing course of intramuscular ACTH over 14 days,

consisting of 80 units for 7 days, 40 units for 4 days, and 20 units for 3 days. To date, retreatment with ACTH has not been evaluated in clinical trials.

- For acute exacerbation of multiple sclerosis, dosage and frequency should be individualized to the patient's needs, taking into account the patient's medical condition, severity of illness, and initial response to treatment. 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 gradually discontinue.

## V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
H.P. Acthar Gel	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 should be gradually tapered over a 2-week period	150 U/m <sup>2</sup> /day
H.P. Acthar Gel, Purified Cortrophin Gel	Acute exacerbation of MS	80-120 units IM/SC daily for 2-3 weeks	120 units/day
H.P. Acthar Gel, Purified Cortrophin Gel	Nephrotic syndrome	40-80 units IM/SC every 24-72 hours	80 units/day

## VI. Product Availability

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

## VII. References

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Nephrotic syndrome: clarified associated conditions; added redirection to cyclophosphamide for IMN and MCD per KDIGO guidelines and prescribing information; references reviewed and updated.	08.06.18	11.18
1Q 2019 annual review: no significant changes; references reviewed and updated.	10.23.18	02.19
1Q 2020 annual review: no significant changes; added mL quantity limits for multiple sclerosis and nephrotic syndrome indications; references reviewed and updated.	11.04.19	02.20
Revised multiple sclerosis approval duration from 4 weeks to 3 weeks and added max vial quantity; revised Appendix D; references reviewed and updated.	05.11.20	08.20
1Q 2021 annual review: no significant changes; references reviewed and updated.	11.04.20	02.21
Added experimental uses previously stated in Appendix D to Section III.	07.28.21	11.21
1Q 2022 annual review: RT4: added Purified Cortrophin Gel to policy; for Acthar added step through Purified Cortrophin Gel; for infantile spasm added requirement that diagnosis is confirmed by EEG per competitor analysis; references reviewed and updated.	09.21.21	02.22

**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.

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