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

**Description**
Repository corticotropin injection (H.P. Acthar® Gel) is adrenocorticotropic hormone (ACTH) in 16% gelatin.

**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
- Acute 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 (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 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/m² per day (divided into twice daily IM injections of 75 U/m²).
   **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®, Plegidy®, Rebif®);
7. Dose does not exceed 120 units per day.
   **Approval duration: 1 month**

**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 contraindicated or clinically significant adverse effects
are experienced: tacrolimus, cyclosporine, mycophenolate, rituximab;
7. Dose does not exceed 80 units 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. Age < 2 years;
   3. Member is responding positively to therapy;
   4. If request is for a dose increase, new dose does not exceed 150 U/m² per day (divided into
twice daily injections of 75 U/m²).
Approval duration: 3 months (one renewal limit)

B. Multiple Sclerosis
   1. Re-authorization is not permitted. H.P. Acthar is 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. If request is for a dose increase, new dose does not exceed 80 units 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.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>tacrolimus (Prograf®)</td>
<td>Nephrotic syndrome: 0.05-0.075 mg/kg/day PO in two divided doses 12 hours apart</td>
<td>0.075 mg/kg/day</td>
</tr>
<tr>
<td>cyclosporine (Neoral®, Sandimmune®)</td>
<td>Nephrotic syndrome: 3.5-5 mg/kg/day PO in two equally divided doses 12 hours apart</td>
<td>5 mg/kg/day</td>
</tr>
<tr>
<td>cyclophosphamide</td>
<td>Nephrotic syndrome: 20 mg/kg/day PO for a 6-month course with alternating monthly cycles of PO and IV corticosteroids</td>
<td>20 mg/kg/day</td>
</tr>
<tr>
<td>mycophenolate (CellCept®)</td>
<td>Nephrotic syndrome: 2-3 g/day PO</td>
<td>3 g/day</td>
</tr>
<tr>
<td>Rituxan® (rituximab)</td>
<td>Nephrotic syndrome: 375 mg/m² IV every week</td>
<td>375 mg/m²/week</td>
</tr>
</tbody>
</table>

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
  - 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
  - Treatment of FDA approved indications accompanied by primary adrenocortical insufficiency or adrenocortical hyperfunction

- 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 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

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>West syndrome (infantile spasms)</td>
<td>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</td>
<td>150 U/m^2/day</td>
</tr>
<tr>
<td>Acute exacerbation of MS</td>
<td>80-120 units IM/SC daily for 2-3 weeks</td>
<td>120 units/day</td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
<td>40-80 units IM/SC every 24-72 hours</td>
<td>80 units/day</td>
</tr>
</tbody>
</table>

VI. Product Availability

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

VII. References


### Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Description</th>
<th>Date Reviwer</th>
<th>Date P&amp;T Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
<td>07.16</td>
<td>09.16</td>
</tr>
<tr>
<td>Converted to new template. Added Nephrotic syndrome and other indications criteria. Updated references.</td>
<td>07.01.17</td>
<td>08.17</td>
</tr>
<tr>
<td>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.</td>
<td>02.06.17</td>
<td>02.18</td>
</tr>
<tr>
<td>Nephrotic syndrome: clarified associated conditions; added redirection to cyclophosphamide for IMN and MCD per KDIGO guidelines and prescribing information; references reviewed and updated.</td>
<td>08.06.18</td>
<td>11.18</td>
</tr>
<tr>
<td>1Q 2019 annual review: no significant changes; references reviewed and updated.</td>
<td>10.23.18</td>
<td>02.19</td>
</tr>
</tbody>
</table>

**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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