Title: H.P. Acthar Gel (repository corticotropin)

- BCBSKS will review Prior Authorization requests

Prior Authorization Form:

Link to Drug List (Formulary):
http://www.bcbsks.com/CustomerService/PrescriptionDrugs/drug_list.shtml

Professional
Original Effective Date: July 1, 2012
Revision Date(s): July 1, 2012;
May 22, 2013; October 12, 2016;
September 1, 2017
Current Effective Date: September 1, 2017

Institutional
Original Effective Date: July 1, 2012
Revision Date(s): July 1, 2012;
May 22, 2013; October 12, 2016;
September 1, 2017
Current Effective Date: September 1, 2017

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member’s benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.
**DESCRIPTION**

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 clinically supported indications including, 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)

<table>
<thead>
<tr>
<th><strong>FDA Approved Indications</strong></th>
<th><strong>Dosing</strong></th>
</tr>
</thead>
</table>
| Infantile Spasm              | **Treatment:** 150 U/m² IM in divided doses daily for 14 days  
**Taper:** 30 U/m² in the a.m. for 3 days; 15 U/m² in the a.m. for 3 days; 10 U/m² in the a.m. for 3 days; and 10 U/m² 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: Adjuvant for short-term administration**
- Psoriatic arthritis
- Rheumatoid arthritis
- Juvenile rheumatoid arthritis
- Ankylosing spondylitis

Usual dose is 40-80 units IM or SC every 24-72 hours. Dosing should be individualized. Tapering may be necessary for discontinuation.

**Collagen Diseases**
- Systemic lupus erythematosus
- Systemic dermatomyositis (polymyositis)

Usual dose is 40-80 units IM or SC every 24-72 hours. Dosing should be individualized. Tapering may be necessary for discontinuation.

**Dermatologic Diseases**
- Severe erythema multiforme
- Steven-Johnson syndrome

Usual dose is 40-80 units IM or SC every 24-72 hours. Dosing should be individualized. Tapering may be necessary for discontinuation.

**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
- Iritis
- Iridocyclitis
- Diffuse posterior uveitis and choroiditis
- Optic neuritis
- Chorioretinitis
- Anterior segment inflammation

Usual dose is 40-80 units IM or SC every 24-72 hours. Dosing should be individualized. Tapering may be necessary for discontinuation.

**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

**POLICY**

**Prior Authorization Criteria for Approval**

A. **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

B. H.P. Acthar Gel will be considered **experimental / investigational** for any other indication.

**Length of Approval:** 6 months for Infantile Spasm

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<th>Agent</th>
<th>Contraindication(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H.P. Acthar gel</td>
<td>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 &lt; 2 years of age with suspected congenital infections, treatment of FDA approved indications when accompanied by primary adrenocortical insufficiency or hyperfunction</td>
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</table>
RATIONALE

H.P. Acthar Gel (repository corticotropin) is an adrenocorticotropic 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 and multiple sclerosis is lacking. According to the manufacturer little data is available for the general indications of rheumatic, collagen, dermatologic, allergic states, ophthalmic, respiratory, and edematous disorders/diseases 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/m² intramuscular twice daily) or prednisone (1mg/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

CODING
The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS
J0800 Injection, corticotropin, up to 40 units

REVISIONS
<table>
<thead>
<tr>
<th>Date</th>
<th>Description</th>
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<tbody>
<tr>
<td>07-01-2012</td>
<td>Policy added to the bcbsks.com web site.</td>
</tr>
<tr>
<td>05-22-2013</td>
<td>Policy Title revised from “H.P. Acthar Gel (repository corticotropin) Prior Authorization Criteria” to “H.P. Acthar Gel (repository corticotropin)”</td>
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<tr>
<td></td>
<td>▪ Added links for Prior Authorization Form, Link to Drug List (Formulary), and For information concerning Prior Authorization Prescription Drugs.</td>
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<tr>
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<td>▪ Added under Prior Authorization Form link “BCBSKS will review Prior Authorization requests effective May xx, 2013.”</td>
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<tr>
<td></td>
<td>Description section updated</td>
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<tr>
<td></td>
<td>In Policy section:</td>
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<td></td>
<td>▪ Revised policy statement from:</td>
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<td>&quot;H.P. Acthar Gel will be approved:</td>
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<tr>
<td></td>
<td>To:</td>
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<td>&quot;A. Repository corticotropin injection may be considered medically necessary for treatment of infantile spasms (West syndrome), when the patient is &lt; 24 months of age.</td>
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<td>B. Use of repository corticotropin injection is considered not medically necessary as treatment of corticosteroid-responsive conditions, except when:</td>
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<tr>
<td></td>
<td>2. There has been an incomplete response to an adequate trial of corticosteroids.</td>
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<tr>
<td></td>
<td>C. Repository corticotropin injection is considered not medically necessary for use in diagnostic testing of adrenocortical function.</td>
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|            | D. Except as noted here, use of repository corticotropin injection is considered experimental / investigational for conditions that are not responsive to corticosteroid
therapy including, but not limited to, use in tobacco cessation, acute gout, and childhood epilepsy."

- Added Policy Guidelines
- Removed Dosing chart as dosing guidelines are referenced in Policy Guidelines

### Rationale section updated

- Added Coding section to include HCPCS code: J0800
- References updated

#### 10-12-2016

**Description section updated**

In Policy section:

- Policy updated to the current policy language for the indications of: infantile spasms and exacerbations of multiple sclerosis in adults, from the following:
  
  "A. Repository corticotropin injection may be considered medically necessary for treatment of infantile spasms (West syndrome), when the patient is < 24 months of age.  
  B. Use of repository corticotropin injection is considered not medically necessary as treatment of corticosteroid-responsive conditions, except when:
  1. There are medical contraindications or intolerance to corticosteroids that are not also expected to occur with use of repository corticotropin injection. This may include, but not be limited to: Multiple Sclerosis, Rheumatic disorders, Collagen diseases, Dermatologic diseases, Allergic states, Ophthalmic diseases, Respiratory diseases, or Edematous state.  
  OR
  2. There has been an incomplete response to an adequate trial of corticosteroids.  
  C. Repository corticotropin injection is considered not medically necessary for use in diagnostic testing of adrenocortical function.  
  D. Except as noted here, use of repository corticotropin injection is considered experimental / investigational for conditions that are not responsive to corticosteroid therapy including, but not limited to, use in tobacco cessation, acute gout, and childhood epilepsy.  

Length of Approval: 6 months"

- Policy Guidelines removed:

  "1. Repository corticotropin injection is one of the agents that can be considered for treatment of infantile spasms as noted in the Rationale section.  
  2. The product information material makes the following comments about dosage:

  - In the treatment of infantile spasms, the recommended dose is 150 U/m2 divided into twice daily intramuscular injections of 75 U/m2. After 2 weeks of treatment, dosing should be gradually tapered and discontinued over a 2-week period.  
  - In the treatment of other disorders and diseases, dosing will need to be individualized depending on the disease under treatment and the medical condition of the patient. It may be necessary to taper the dose.  
  - Repository corticotropin is generally more costly than alternative agents but has not been shown to lead to improved outcomes compared to those obtained with alternatives for some indications""

#### Rationale section updated

- References updated

#### 09-01-2017

**Policy published 08-01-2017. Policy effective 09-01-2017.**

**Description section updated**

In policy section:

- In Item 2 added “BOTH of the following” and removed “ONE of the following:”
- Removed multiple sclerosis indication by removing the following policy language:

  "Multiple sclerosis AND  
  i. The patient is experiencing an acute exacerbation  
  ii. If indicated, the patient is currently on a disease modifying drug (DMD) (e.g. interferon beta-1a [Avonex, Rebif], peginterferon beta-1a [Plegridy], interferon beta-1b [Betaseron, Extavia], glatiramer acetate [Copaxone, Glatopa], natalizumab [Tysabri], mitoxantrone"
Novantrone, fingolimod [Gilenya], dimethyl fumarate [Tecfidera], teriflunomide [Aubagio], alentuzumab [Lemtrada]) to control disease progression OR has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a DMD AND iii. The patient has failed corticosteroid therapy within the last 30 days or has an FDA labeled contraindication to corticosteroid therapy (e.g. Solu-Medrol [methylprednisolone] 1gm IV for 3-5 days)

- Added “H.P. Acthar Gel will be considered experimental / investigational for any other indication.”
- In Length of Approval removed “1 month for an acute exacerbation of multiple sclerosis”
- Updated FDA Approved Indication and Dosing chart

<table>
<thead>
<tr>
<th>Rationale section updated</th>
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<tbody>
<tr>
<td>References updated</td>
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**REFERENCES**

4. Deleted
5. Deleted
6. Deleted
7. Deleted
8. Deleted