Medical Policy

BlueCross BlueShield of Kansas
An independent licensee of the Blue Cross Blue Shield Association

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

- **BCBSKS will review Prior Authorization requests**

Prior Authorization Form:
http://www.bcbsks.com/CustomerService/Forms/pdf/15-17_predeterm_request_frm.pdf

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
Current Effective Date: October 12, 2016

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

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.

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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 guidelines 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 and acute exacerbations of multiple sclerosis. Criteria require that patients do not have any FDA labeled contraindications to use H.P. Acthar Gel and that for an acute exacerbation of multiple sclerosis, the patient has had an incomplete response to a trial of corticosteroids.

Target Drugs

- **H.P. Acthar Gel** (repository corticotropin)

FDA Approved Indications	Dosing
▪ Infantile Spasm ▪ Acute exacerbation of Multiple Sclerosis	**Treatment:** 150 U/m^2 IM in divided doses daily for 14 days **Taper:** 30 U/m^2 in the a.m. for 3 days; 15 U/m^2 in the a.m. for 3 days; 10 U/m^2 in the a.m. for 3 days; and 10 U/m^2 every other a.m. for 6 days
	80-120 units IM or SC daily for 2-3 weeks
Rheumatic Disorders: Adjunctive 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.

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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

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. The patient has been diagnosed with **ONE** of the following:
   a. Infantile spasms **AND**
      i. The patient is < 24 months of age
      OR
   b. Multiple sclerosis **AND**
      i. The patient is experiencing an acute exacerbation
      AND
      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], alemtuzumab [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)
   AND
3. The dose is within the FDA labeled dosing for the requested indication.

Length of Approval: 6 months for Infantile Spasm
1 month for an acute exacerbation of multiple sclerosis

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FDA Approved Indications	Dosing
Infantile Spasm	**Treatment:** 150 U/m^2 IM in divided doses daily for 14 days **Taper:** 30 U/m^2 in the a.m. for 3 days; 15 U/m^2 in the a.m. for 3 days; 10 U/m^2 in the a.m. for 3 days; and 10 U/m^2 every other a.m. for 6 days
Acute exacerbation of Multiple Sclerosis	80-120 units IM or SC daily for 2-3 weeks

U- units; IM- intramuscularly; SC- subcutaneously

Agent	Contraindication(s)
H.P. Acthar gel	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 < 2 years of age with suspected congenital infections, treatment of FDA approved indications when accompanied by primary adrenocortical insufficiency or hyperfunction

RATIONALE

H.P. Acthar Gel (repository corticotropin) is an adrenocorticotropin 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/m^2 intramuscular twice daily) or prednisone (1 mg/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]

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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]

Multiple Sclerosis:
The FDA approval of corticotropin (ACTH) for the treatment of acute relapse in multiple sclerosis (MS) is based on available literature and not based on specific clinical trials conducted by the manufacturer for this indication.

American Academy of Neurology Clinical Practice Guidelines on disease modifying therapies in multiple sclerosis (2002, reaffirmed 2008) recommend glucocorticoids for the treatment of acute attacks of MS based on Class I and Class II studies. The guidelines also state that there is not compelling evidence to indicate that clinical benefits are influenced by route of administration, glucocorticoid prescribed, or the dosage of the glucocorticoid. Acthar is not referenced in these guidelines.[8]

The NICE Guidelines for the Management of multiple sclerosis in primary and secondary care recommend intravenous methylprednisolone or high dose oral methylprednisolone daily for 3 to 5 days.[6] NICE guidelines do not recommend the use of corticosteroids for treatment of frequent (> 3 times per year) or prolonged (longer than 3 weeks) acute exacerbations.

The European Federation of Neurological Societies (EFNS) guidelines on the treatment of MS relapses recommend intravenous or oral methylprednisolone in a dose of at least 500 mg daily for 5 days as short term therapy. These same guidelines note that glucocorticoid treatment is the first-line treatment for MS relapses in North American and European guidelines.[7]

A Cochrane Review (2009) included 6 randomized, blinded controlled trials with 377 participants overall. All the trials included in the review did show a consistent pattern suggesting a benefit of ACTH or methylprednisolone (MP) treatment with respect to improving acute exacerbation of symptoms within the first 5 weeks of treatment. The authors determined there is insufficient evidence to determine if steroids or ACTH treatment prevented new exacerbations and worsening of long-term disability.[5]

A study conducted by Thompson AJ et al, compared intravenous (IV) methylprednisolone (MP) and H.P. Acthar gel in the treatment of acute relapse in MS patients. In this double-blind, randomized, controlled trial 29 patients received 1g IV daily for 3 days of MP and 32 patients

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received a tapering course of intramuscular ACTH over 14 days. The groups were well matched with no significant differences. Mean scores and mean change in scores for each functional system and for overall disability was compared at each assessment. The results indicate clear improvement in both groups but no significant difference between the 2 groups in either rate of recovery or final outcome at 3 months.[4]

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

07-01-2012	Policy added to the bcbsks.com web site.
05-22-2013	Policy Title revised from “H.P. Acthar Gel (repository corticotropin) Prior Authorization Criteria” to “H.P. Acthar Gel (repository corticotropin)”
	▪ Added links for Prior Authorization Form, Link to Drug List (Formulary), and For information concerning Prior Authorization Prescription Drugs. ▪ Added under Prior Authorization Form link "BCBSKS will review Prior Authorization requests effective May xx, 2013."
	Description section updated
	In Policy section: ▪ Revised policy statement from: "H.P. Acthar Gel will be approved: 1. when the patient has been diagnosed with Infantile spasms AND 2. the patient is < 24 months of age" To: "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

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	are not also expected to occur with use of repository corticotropin injection. As reflected in the description section 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." ▪ 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

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	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

REFERENCES

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