09-J1000-15

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Subject: H.P. Acthar® Gel (Repository corticotropin)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Repository corticotropin (H.P. Acthar® Gel repository injection) is 39-amino-acid peptide and is a natural product derived from a bovine or porcine source of the adrenocorticotropic hormone (ACTH). It works by stimulating the adrenal cortex to secrete cortisol, corticosterone, aldosterone and a number of other androgenic substances. In the body, corticotropin-releasing hormone (CRH) from the hypothalamus stimulates the release of ACTH from the anterior pituitary gland. Conversely, high levels of cortisol in the serum act via a negative feedback mechanism to decrease the output of ACTH. Repository corticotropin injection was originally approved by the US Food and Drug Administration (FDA) in 1952 for a broad range of corticosteroid-responsive conditions including rheumatic, collagen, dermatologic, allergic states, ophthalmic, respiratory, and edematous states. Current labeled indications include acute multiple sclerosis exacerbations, rheumatic disorders, collagen diseases, dermatologic diseases, allergic states, ophthalmologic diseases, respiratory diseases and edematous states. Although there are a variety diseases and disorders for which it may be used, corticosteroids remain the treatment of choice in corticosteroid-responsive conditions. This in large part due to the lack of clinical studies comparing the effectiveness of repository corticotropin gel to corticosteroids in corticosteroid responsive conditions and that there is no reliable evidence of the effectiveness in persons who have failed to respond to corticosteroids. Furthermore, repository corticotropin has the potential for inducing significant adverse effects due to its effect on endogenous cortisol production.

In October 2010, repository corticotropin was approved by the US Food and Drug Administration (FDA) as monotherapy for the treatment of infantile spasms (West Syndrome) in infants and children less than two years of age. West Syndrome is a rare epileptic disorder and consists of three main characteristics: infantile spasms, mental retardation, and hypsarrhythmia, a specific abnormal pattern. Hypsarrhythmia is detected by an electroencephalogram (EEG) and is characterized by slow waves of high voltage and random spikes that vary in duration and location. Approximately 90% of cases are diagnosed during an

infant's first year of life. Although West Syndrome is a rare condition, it is associated with a poor prognosis for normal mental development. The use of repository corticotropin in infantile spasms associated with West Syndrome is supported in practice guidelines coauthored by the American Academy of Neurology (AAN) and the child Neurology Society, and it is considered "probably effective" for the short term treatment of infantile spasms. The guidelines also state that low-dose repository corticotropin is probably as effective as high-dose and that there is insufficient evidence to determine whether other forms of traditionally dosed corticosteroids (e.g., prednisone 2 mg/kg/day) are as effective for short-term treatment. To date, a randomized, prospective head-to-head study comparing ACTH to corticosteroids has not been conducted. In a recent pilot study by Hussain and colleagues, the effectiveness of very high-dose prednisolone (4-8 mg/kg/day) was evaluated. Subjects (n=22) with video-EEG confirmed infantile spasms were administered very-high dose prednisolone for 2 weeks and were monitored for complete response. ACTH was administered at the end of the 2 week period in subjects who did not respond. Overall, 50% (11/22) of subjects had a complete response to very-high dose prednisolone. Of the remaining 11 subjects who did not respond, 36% (4/11) demonstrated a complete response following ACTH administration. Although there are several limitations to this study, including a small number of subjects, lack of a control arm, and lack of randomization, this trial supports a clinical approach of providing prednisolone as initial treatment followed by ACTH as rescue therapy.

POSITION STATEMENT:

NOTE: Provider is required to submit medical records (e.g., history and physical, consultation note, office notes) as justification that criteria are met.

Initiation of repository corticotropin (H.P. Acthar gel) **meets the definition of medical necessity** when all of the following criteria are met:

1. Indication for use is infantile spasms (West Syndrome)
2. Member is less than 24 months of age
3. The member does not have any of the following:
    a. Scleroderma
    b. Osteoporosis
    c. Systemic Fungal Infection
    d. Ocular herpes simplex
    e. Recent surgery (e.g., within the previous 30 days)
    f. History of or the presence of a peptic ulcer
    g. Congestive heart failure
    h. Uncontrolled hypertension
    i. Sensitivity to proteins of porcine origin
4. Dose does not exceed 150 units/m^2/day

Duration of approval: 28 days

Continuation of repository corticotropin (H.P. Acthar gel) **meets the definition of medical necessity** when all of the following criteria are met:

1. Indication for use is infantile spasms (West Syndrome)
2. Member is less than 24 months of age
3. The member does not have any of the following:
    a. Scleroderma
    b. Osteoporosis
    c. Systemic Fungal Infection
    d. Ocular herpes simplex
    e. Recent surgery (e.g., within the previous 30 days)
    f. History of or the presence of a peptic ulcer
    g. Congestive heart failure
    h. Uncontrolled hypertension
    i. Sensitivity to proteins of porcine origin
4. Dose does not exceed 150 units/m^2/day

Duration of approval: 28 days

Repository corticotropin (H.P. Acthar gel) does not meet the definition of medical necessity for all other indications, including the following (not an all-inclusive list):

- Amyotrophic lateral sclerosis
- Dermatopolymyositis
- Multiple sclerosis
- Optic neuritis
- Nephrotic syndrome (including focal segmental glomerulo-sclerosis, idiopathic membranous nephropathy, IgA nephropathy, membrano-proliferative glomerulo-nephritis, and monoclonal diffuse proliferative glomerulo-nephritis)
- Rheumatoid arthritis
- Systemic lupus erythematosus

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved:

Infantile Spasms - 75 Units/m2 IM twice daily for 2 weeks; After 2 weeks of treatment, dosing should be gradually tapered and discontinued over a 2 week period

Dosage Adjustments: specific guidelines for dosage adjustments in hepatic or renal impairment are not available; it appears that no dosage adjustments are needed.

Drug Availability: corticotropin gel is available as a 5 mL multi-dose vial containing 80 USP units per mL.

PRECAUTIONS:

CONTRAINDICATIONS:

- Corticotropin gel should be administered as an intramuscular injection **ONLY** and should **NEVER** be administered intravenously.
- Corticotropin gel is contraindicated in members with any of the following conditions:
    - Scleroderma
    - Osteoporosis
    - Systemic Fungal Infection
    - Ocular herpes simplex
    - Recent surgery
    - History of or the presence of a peptic ulcer
    - Congestive heart failure
    - Uncontrolled hypertension
    - Sensitivity to proteins of porcine origin
- Do not administer live or live attenuated vaccines in members receiving immunosuppressive doses of corticotropin gel
- Do not administer corticotropin gel to children less than 2 years of age with a suspected congenital infection
- Do not administer in members with primary adrenocortical insufficiency or adrenocortical hyperfunction.

WARNINGS

Infection: corticotropin gel administration may increase a member's susceptibility to a new infection and increase the risk of exacerbation, dissemination, or reactivation of latent infections. Signs and symptoms of infection may be masked.

Adrenal Insufficiency: prolonged therapy may result in adrenal insufficiency; monitor members for effects of hypothalamic-pituitary-axis (HPA) suppression after stopping treatment.

Cushing's Syndrome: may occur after prolonged therapy; monitor for signs and symptoms.

Elevated blood pressure, salt and water retention, hypokalemia: monitor blood pressure and electrolytes.

Gastrointestinal perforation and bleeding: there is a risk for gastric ulcers and bleeding. Members with certain GI disorders may be at greater risk. Members should be monitored for signs of perforation and bleeding; additionally, signs and symptoms may be masked by therapy.

Behavioral and Mood Disturbances: May include euphoria, insomnia, mood swings, personality changes, severe depression and psychosis. Existing conditions may be aggravated.

Comorbid disease: corticotropin gel may worsen the symptoms of diabetes and myasthenia gravis.

Ophthalmic effects: monitor for cataracts, infections and glaucoma.

Immunogenicity potential: neutralizing antibodies with chronic administration may lead to a loss of endogenous ACTH activity.

Hypothyroidism or Liver Cirrhosis: therapy may result in an enhanced effect of hypothyroidism or liver cirrhosis.

Growth and physical development: pediatric members on long-term therapy should be monitored for negative effects on growth and physical development.

Osteoporosis: therapy may result in decreased bone density; members receiving long-term therapy should be monitored for signs of osteoporosis.

Pregnancy: corticotropin gel has demonstrated an embryocidal effect. Female members should be apprised of the potential harm to the fetus.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J0800	Injection, corticotropin, up to 40 units

ICD-10 Diagnosis Codes That Support Medical Necessity

G40.821	Epileptic spasms, not intractable, with status epilepticus
G40.822	Epileptic spasms, not intractable, without status epilepticus
G40.823	Epileptic spasms, intractable, with status epilepticus
G40.824	Epileptic spasms, intractable, without status epilepticus

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage: Medical necessity is determined using any applicable NCD or LCD and then Step therapy Requirements for Medicare Outpatient (Part B) Medications outlined in Policy (09-J3000-39).

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline

DEFINITIONS:

ACTH (adrenocorticotrophic hormone): a 39–amino-acid anterior pituitary hormone, one of the derivatives of pro-opiomelanocortin; it acts primarily on the adrenal cortex, stimulating its growth and the secretion of corticosteroids. Its production is increased during times of stress. It is also a preparation of the hormone derived from mammals used for food, administered intravenously for diagnostic testing of adrenocortical function.

Hypsarrhythmia: chaotic abnormal brain wave patterns.

Pro-opiomelanocortin: the 31,000 dalton prohormone that is the precursor of corticotropin, the lipotropins, the melanocyte-stimulating hormones, and the endorphins, all of which are produced by posttranslational proteolytic cleavage in cell types that produce these hormones.

RELATED GUIDELINES:

None

OTHER:

None applicable.

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 01/09/19.

GUIDELINE UPDATE INFORMATION:

01/15/10	New Medical Coverage Guideline.
04/15/10	Review and revision of guideline; consisting of updating references.
04/15/11	Review and revision of guideline; consisting of updating the precautions and references.
04/15/12	Review and revision of guideline; consisting of removing diagnostic of adrenocortical function as covered indication, updating precautions and references.
02/15/13	Review and revision to guideline; consisting of reformatting position statement; revising and reformatting description, dosage/administration and precautions sections; updated references.
04/15/13	Revision to guideline; consisting of reformatting and revising position statement; updating program exception information; adding pertinent definitions and updating references.
11/15/13	Review and revision to guideline; consisting of revising position statement.
02/15/14	Review and revision to guideline; consisting of updating position statement, related guidelines, program exceptions, and references.
02/15/15	Review and revision to guideline; consisting of position statement, dosage/administration, references.
08/15/15	Revision to guideline; consisting of position statement.
10/01/15	Revision consisting of update to Program Exceptions section.
11/01/15	Revision: ICD-9 Codes deleted.
02/15/16	Review and revision to guideline; consisting of updating position statement and references.
02/15/17	Review and revision to guideline; consisting of updating references.
02/15/18	Review and revision to guideline; consisting of updating references.
02/15/19	Review and revision to guideline; consisting of updating references.
07/15/19	Update to Program Exceptions.