BlueCross BlueShield of Louisiana

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Repository Corticotropin Injection (ACTH Gel, H.P. Acthar Gel®)

Policy # 00230
Original Effective Date: 07/16/2008
Current Effective Date: 09/17/2014

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Vigabatrin (Sabril®)‡ is addressed in medical policy 00244.

When Services Are Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider repository corticotropin injection for the treatment of infantile spasms (West's syndrome) and multiple sclerosis (MS) to be **eligible for coverage**.

Patient Selection Criteria
Coverage eligibility for the use of repository corticotropin injection will be considered when the following criteria are met:

- Patient has a diagnosis of infantile spasms AND is less than 2 years of age; OR
- Patient has a diagnosis of an acute exacerbation of multiple sclerosis (MS) AND repository corticotropin injection is NOT being used for pulse therapy (defined as use on a once monthly or routine basis to prevent multiple sclerosis [MS] exacerbations); AND
    - Patient has tried and failed high dose intravenous (IV) corticosteroids (e.g. methylprednisolone 500mg to 1000mg intravenous [IV] daily for 3 to 5 days); OR
      *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
    - Patient has experienced a severe or limiting adverse effect to the high-dose corticosteroids
      *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary
The use of repository corticotropin injection as treatment of steroid-responsive conditions not mentioned in the above patient selection criteria is considered to be **not medically necessary.****

The use of repository corticotropin injection in patients with acute exacerbations of multiple sclerosis (MS) without having tried and failed high dose intravenous (IV) corticosteroids (e.g. methylprednisolone 500mg to 1000mg intravenous [IV] daily for 3 to 5 days) OR if the patient has NOT experienced a severe or limiting adverse effect to high-dose corticosteroids is considered to be **not medically necessary.****

The use of repository corticotropin injection in diagnostic testing of adrenocortical function is considered to be **not medically necessary.****

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When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of repository corticotropin injection for conditions that are not responsive to corticosteroid therapy (including, but not limited to, use in tobacco cessation, acute gout and childhood epilepsy) OR for any non-FDA approved indication to be **investigational.***

Background/Overview

Repository corticotropin injection (H.P. Acthar® † Gel, Questcor, Union City, CA)‡ is a purified, sterile preparation of the natural form of adrenocorticotropic hormone (ACTH) in gelatin to provide a prolonged release after intramuscular or subcutaneous injection. Adrenocorticotropic hormone works by stimulating the adrenal cortex to produce cortisol, corticosterone, and a number of other hormones.

H.P. Acthar Gel is an ACTH analogue indicated as monotherapy for the treatment of infantile spasms in infants and children under 2 years of age. It is also indicated for the treatment of exacerbations of multiple sclerosis in adults. According the package insert, H.P. Acthar gel may be used for the following disorders and diseases: rheumatic, collagen, dermatologic, allergic states, ophthalmic, respiratory and edematous states.

Contraindications for use of this agent include 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.

Unlike previous versions, the 2010 product label does not mention the use of repository corticotropin injection for diagnostic testing of adrenocortical function.

Cosyntropin (Cortosyn® †, Amphastar)‡, a synthetic form of ACTH, is created by isolating the first 24 amino acids from ACTH peptide. Unlike the natural form of ACTH, which is given intramuscularly or subcutaneously, Cortosyn should only be given intravenously. A depot formulation of cosyntropin (Synacthen Depot) is not approved by the U.S. Food and Drug Administration (FDA) for treating infantile spasms. However, it is available through a compassionate-use program through the specialty pharmacy Caligor Rx in New York.

West Syndrome/Infantile Spasms
West syndrome is a rare epileptic disorder of early infancy (90% of cases are diagnosed the first year of life) consisting of three main characteristics; infantile spasm, mental retardation, and hypsarrhythmia, a specific abnormal pattern on EEG. Often the term infantile spasms is used synonymously with West syndrome. Infantile spasms are characterized by an initial contraction phase followed by a more sustained tonic phase.

Another treatment option for infantile spasms is Vigabatrin (Sabril, Lundbeck, Inc.), which is an oral solution. Sabril is indicated as monotherapy for pediatric patients with infantile spasms for whom the potential benefits outweigh the potential risk of vision loss.

Multiple Sclerosis
Multiple sclerosis is typically characterized by patches of demyelination in the brain and spinal cord. Symptoms include visual and oculomotor abnormalities, spasticity, urinary dysfunction, weakness, and cognitive impairment. It is thought to be caused by an immunologic mechanism. Patients with MS can experience an exacerbation which can cause new symptoms or can worsen old symptoms. Multiple sclerosis exacerbations are typically treated with intravenous corticosteroids over a 3-5 day period. Acute MS exacerbations generally only occur once yearly for those with relapsing forms who are receiving optimal disease-modifying agents.

FDA or Other Governmental Regulatory Approval

U.S. FDA
Acthar is currently approved in the U.S. for the treatment of MS exacerbations, infantile spasms, and other conditions.

Centers for Medicare and Medicaid Services (CMS)
No national coverage determination.

Rationale/Source

Infantile spasms
The effectiveness of H.P. Acthar Gel as a treatment for infantile spasms was demonstrated in a single blinded (video EEG Interpreter blinded) clinical trial In which patients were randomized to receive either a 2 week course of treatment with H.P. Acthar Gel (75 U/m^2) intramuscular twice daily or prednisone (1 mg/kg by mouth 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, rated by an investigator blinded to treatment. Thirteen of 15 patients (86.7%) responded to H.P. Acthar Gel as compared to 4 of 14 patients (28.6%) given prednisone ($p < 0.002$). The 2-week treatment was followed by a 2-week period of taper. Nonresponders to the prednisone treatment were eligible to receive H.P. Acthar Gel treatment. Seven of 8 patients (87.5%) responded to H.P. Acthar Gel after not responding to prednisone. Similarly, the 2 nonresponder patients from the H.P. Acthar Gel treatment were eligible to receive treatment with prednisone. One of the 2 patients (50%) responded to the prednisone treatment after not responding to H.P. Acthar Gel.

A supportive single-blind, randomized clinical trial comparing high-dose, long-duration treatment (150U/m^2 once daily for 3 weeks, n = 30) of H.P. Acthar Gel with low-dose, short-duration treatment (20U once daily for 2 weeks, n = 29) for the treatment of infantile spasms was also evaluated in infants and children less than 2 years of age. Nonresponders (defined as in the previously described study) in the low-dose group received a dose escalation at 2 weeks to 30U once daily. Nominal statistical superiority of the high dose treatment, as

compared to the low dose treatment, was observed for cessation of spasms but not for the resolution of hypsarrhythmia.

In 2012 the American Academy of Neurology (AAN) and the Child Neurology Society updated the evidence-based guideline for the medical treatment of infantile spasms. The guidelines note that ACTH is a first-line agent for the short-term treatment of infantile spasms. The Infantile Spasms Working Group (ISWG) published a US consensus report on infantile spasms in 2010. Data regarding ACTH use in infantile spasms were detailed and it was determined that ACTH is an effective first-line therapy for infantile spasms.

Acute Exacerbations of Multiple Sclerosis
Acthar is indicated for the treatment of exacerbations of MS in adults. Acthar has been studied in patients with acute exacerbations of MS and short-term use, usually given IM or SC for 14 or fewer days, led to benefits in signs and symptoms of MS. A double-blind, randomized controlled trial found that ACTH given IM over 14 days had similar efficacy in acute exacerbations of MS as methylprednisolone given as 1 gram IV daily for 3 days. The National MS Society has a document regarding HP Acthar gel. Acthar may have a role in selected patients, such as patients having difficulty receiving IV medication due to poor venous access. In the professional opinion of specialist physicians reviewing the data, we have adopted these criteria.

Other potential uses of repository corticotrophin injection
The recommended authorization criteria address the use of Acthar in infantile spasms and MS exacerbations in adults. Regarding Acthar's other uses, data and guidelines do not suggest that Acthar has a substantial role in therapy. Further data are needed before use in other areas can be recommended.

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Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2013 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J0800
ICD-9 Diagnosis	255.0, 340, 345.60, 345.61
ICD-9 Procedure	No codes

Policy History

Original Effective Date: 07/16/2008
Current Effective Date: 09/17/2014

07/02/2008	Medical Director review
07/16/2008	Medical Policy Committee approval. New policy.
07/02/2009	Medical Director review
07/22/2009	Medical Policy Committee approval. No change to coverage.
12/04/2009	Medical Policy Committee approval
12/16/2009	Medical Policy Implementation Committee approval. Title changed from "ACTH Gel (Adrenocorticotropic Hormone)" to "Repository Corticotropin Injection (ACTH Gel, H.P. Acthar® Gel)". No change to coverage eligibility.

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07/01/2010	Medical Policy Committee approval
07/21/2010	Medical Policy Implementation Committee approval. Acute gout and childhood epilepsy added as investigational conditions.
12/01/2010	Medical Policy Committee review
12/15/2010	Medical Policy Implementation Committee approval. Added "in infants and children less than two years of age" to repository corticotropin injection for the treatment of infantile spasms (West's syndrome) coverage eligibility statement.
12/08/2011	Medical Policy Committee review
12/21/2011	Medical Policy Implementation Committee approval. No change to coverage.
12/06/2012	Medical Policy Committee review
12/19/2012	Medical Policy Implementation Committee approval. No change to coverage.
09/05/2013	Medical Policy Committee review
09/18/2013	Medical Policy Implementation Committee approval. Policy now states that covered indications include infantile spasms and multiple sclerosis only. Updated background, source, rationale, investigational, and not medically necessary sections.
09/04/2014	Medical Policy Committee review
09/17/2014	Medical Policy Implementation Committee approval. No change to coverage.

Next Scheduled Review Date: 09/2015

*****Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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