Repository Corticotropin Injection

**DISCLAIMER**
Our medical policies are designed for informational purposes only and are not an authorization, explanation of benefits or a contract. Receipt of benefits is subject to satisfaction of all terms and conditions of the coverage. Medical technology is constantly changing, and we reserve the right to review and update our policies periodically.

**POLICY**
Repository corticotropin injection may be considered **medically necessary** for the treatment of infantile spasms (West syndrome).

Use of repository corticotropin injection is considered **investigational** as a treatment of corticosteroid-responsive conditions (see Policy Guidelines section).

Except as noted above, use of repository corticotropin injection is considered **investigational** for conditions that are not responsive to corticosteroid therapy including, but not limited to, use in tobacco cessation, acute gout, and childhood epilepsy.

Repository corticotropin injection is considered **investigational** for use in diagnostic testing of adrenocortical function.

**POLICY GUIDELINES**
Some patients may have medical contraindications or intolerance to corticosteroids that are not expected to occur with use of repository corticotropin injection, and who therefore may benefit from repository corticotropin injections. This situation is not common.

Product information provides the following on dosage of H.P. Acthar Gel for treatment of infantile spasms:

- 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).

H.P. Acthar gel is used for intramuscular or subcutaneous injection and should never be used intravenously.
BENEFIT APPLICATION

BLUECARD/NATIONAL ACCOUNT ISSUES
State or federal mandates (eg, Federal Employee Program) may dictate that certain U.S. Food and Drug Administration–approved devices, drugs, or biologics may not be considered investigational, and thus these devices may be assessed only by their medical necessity.

According to the manufacturer’s website, beginning in 2007, H.P. Acthar Gel is only available through specialized pharmacy distribution (ie, it is no longer available from traditional pharmaceutical wholesalers or retail pharmacies).

BACKGROUND

REPOSITORY CORTICOTROPIN INJECTION
Repository corticotropin injection (H.P. Acthar Gel) 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. ACTH is produced and secreted by the pituitary gland; H.P. Acthar Gel uses ACTH obtained from porcine pituitaries. ACTH works by stimulating the adrenal cortex to produce cortisol, corticosterone, and a number of other hormones.

REGULATORY STATUS
In 1952, H.P. Acthar® Gel (Questcor Pharmaceuticals/Mallinckrodt Pharmaceuticals) was approved by the U.S. Food and Drug Administration. The original product label included at least 19 separate conditions, including infantile spasms. At one time, this product was indicated as an injection for diagnostic testing of adrenocortical function. In 2010, this indication was removed with an update to the product label.

Indications
H.P. Acthar® Gel was approved by the Food and Drug Administration before the requirement that companies provide evidence of clinical efficacy. Table 1 summarizes the current prescribing indications and usage for Acthar® Gel.1

<table>
<thead>
<tr>
<th>Table 1. Indications for Repository Corticotropin Injection</th>
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<tbody>
<tr>
<td>Indication</td>
</tr>
<tr>
<td>Infantile spasms</td>
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<tr>
<td>Multiple sclerosis</td>
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<tr>
<td>Rheumatic disorders</td>
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<tr>
<td>Collagen diseases</td>
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<tr>
<td>Dermatologic diseases</td>
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<tr>
<td>Allergic states</td>
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<td>Respiratory diseases</td>
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<td>Edematous state</td>
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Controlled trials have shown H.P. Acthar Gel to be effective in speeding the resolution of acute exacerbations of multiple sclerosis. However, there is no evidence that it affects the ultimate outcome or natural history of the disease.

Keratitis; iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis; anterior segment inflammation.

Without uremia of the idiopathic type or due to lupus erythematosus.

Diagnostic testing of adrenocortical function, known as the ACTH test, is typically done with synthetic ACTH. Synthetic ACTH products have been approved by the Food and Drug Administration for this purpose.

**Adverse Events**

Contraindications for the 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.

Repository corticotropin injection has potential adverse events similar to those that occur with other steroid medications such as an elevated blood pressure, a decrease in bone density, new infections (or activation of a previous infection), and overproduction of cortisol, which can cause symptoms of Cushing syndrome.

**RATIONALE**

This evidence review was created in February 2008 and has been updated regularly with searches of the MEDLINE database. The most recent literature update was performed through August 23, 2018.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

**INFANTILE SPASMS**

**Clinical Context and Test Purpose**

The purpose of repository corticotropin injection is to provide a treatment option that is an alternative to or an improvement on existing therapies in patients with infantile spasms.

The question addressed in this evidence review is: Does the use of repository corticotropin injection to treat infantile spasms improve the net health outcome?
The following PICOTS were used to select literature to inform this review.

**Patients**
The relevant population of interest is individuals with infantile spasms. This is a rare epileptic disorder of infancy (90% of cases are diagnosed in the first year of life). When infantile spasms are accompanied by neurodevelopmental regression and electroencephalogram findings of hypsarrhythmia, the condition is known as West syndrome.

**Interventions**
The therapy being considered is repository corticotropin injection.

**Comparators**
The following therapies are currently being used to treat infantile spasms: prednisolone and vigabatrin oral solution. Treatment may also include anticonvulsant drugs.

**Outcomes**
The general outcomes of interest are reductions in symptoms and improvements in disease status.

**Timing**
Follow-up at 6, 12, and 24 months is of interest for repository corticotropin injection to monitor for changes in symptoms and disease status.

**Setting**
Patients with infantile spasms are actively managed by neurologists and pediatricians in an outpatient setting.

**Study Selection Criteria**
Evidence that repository corticotropin injection (ie, natural adrenocorticotropic hormone [ACTH] injection) is a reasonable alternative to corticosteroid treatment requires controlled studies demonstrating superiority or noninferiority of repository corticotropin injection to corticosteroids as first-line treatment, or controlled studies showing comparable efficacy of with fewer adverse effects. RCTs are crucial to avoid noncomparability of treatment groups. Alternatively, for patients unable to tolerate corticosteroids, the most appropriate study design would be a controlled study comparing repository corticotropin injection with placebo.

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

**Systematic Reviews**
A Cochrane review by Hancock et al (2013) assessed medication treatment of infantile spasms, including ACTH. Reviewers identified 18 RCTs investigating 12 medications. The studies were deemed to be of poor quality, with more than half of them failing to report the method of randomization—and nearly all of them consisting of fewer than 100 participants. Five studies compared treatment using ACTH with
another medication. Three trials assessed natural ACTH and the others evaluated synthetic ACTH. Reviewers conducted several quantitative meta-analyses that did not differentiate between natural and synthetic ACTH. A pooled analysis of 3 studies found that symptom resolution occurred in 30 (67%) of 45 patients responding to vigabatrin and 40 (82%) of 49 patients responding to ACTH. The difference between groups was statistically significant (odds ratio, 0.38; 95% confidence interval, 0.15 to 0.99). The limited evidence from RCTs suggested that hormonal treatment (prednisolone, tetracosactide depot, ACTH) resolved infantile spasms faster than vigabatrin and resolved the condition in more children, but long-term developmental and epilepsy outcomes are unknown.

**Prospective Studies**

In addition to the RCTs evaluated in the Cochrane review, findings from a prospective national database of children with infantile spasms were published by Knupp et al (2016). A total of 230 infants were included in the database, and 94 responded to initial treatment for infantile spasms. Response rates by type of treatment were 55 (55%) for ACTH, 21 (39%) for oral corticosteroids, 17 (36%) for vigabatrin, and 2 (9%) for “other” (p<0.001). The type of ACTH, natural or synthetic, was not specified and the groups might have differed on characteristics that affect outcomes. Some significant differences between groups were identified (eg, length of time from diagnosis to the start of treatment, history of prior seizures). In logistic regression models controlling for some potential confounding factors, children on ACTH remained more likely to respond to treatment than other children. However, there might have been residual confounding on unmeasured characteristics.

**Section Summary: Infantile Spasms**

There is some evidence from several RCTs and a prospective database that natural and synthetic ACTH have greater short-term efficacy in resolving infantile spasms than other medications (eg, vigabatrin, oral corticosteroids). However, most of the RCTs were small or of poor quality, and only a few evaluated natural ACTH.

**CORTICOSTEROID-RESPONSIVE CONDITIONS**

**Clinical Context and Test Purpose**

The purpose of repository corticotropin injection is to provide a treatment option that is an alternative to or an improvement on existing therapies in patients with corticosteroid-responsive conditions.

The question addressed in this evidence review is: Does the use of repository corticotropin injection to treat corticosteroid-responsive conditions improve the net health outcome?

The following PICOTS were used to select literature to inform this review.

**Patients**

The relevant population of interest is individuals with corticosteroid-responsive conditions. Corticosteroid therapy is common in therapeutic regimens treating autoimmune and rheumatologic disorders.

**Interventions**

The therapy being considered is repository corticotropin injection.

**Comparators**

The following therapies are currently being used to treat corticosteroid-responsive conditions: synthetic corticosteroids.
Outcomes
The general outcomes of interest are reductions in symptoms and improvements in disease status.

Timing
Treatment duration and follow-up of at least 6 months for repository corticotropin injection is necessary to monitor for changes in symptoms and disease status.

Setting
Patients with corticosteroid-responsive conditions are actively managed by dermatologists, rheumatologists, and primary care providers in an outpatient setting.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Randomized Controlled Trials
Controlled studies were identified for treatment of multiple sclerosis with ACTH, but not treatment of other corticosteroid-responsive conditions. Several RCTs, published in the 1960s and early 1970s, compared ACTH with placebo for the treatment of acute exacerbations of multiple sclerosis. A trial described in recent review articles as the most rigorous of these RCTs was published by Rose et al (1969, 1970).4,5 This multicenter, double-blind study included 197 patients. Patients were randomized to intramuscular injections of ACTH gel or placebo during a 2-week hospitalization for acute exacerbations of multiple sclerosis. The trial used Depo-ACTH and placebo, both prepared by Upjohn. A review article by Berkovich (2013) found that ACTH hastened improvement in symptoms but the differences between the ACTH and placebo-treated patients were less marked as the dosage of ACTH was reduced during the second week of treatment.6

Use of ACTH for treating multiple sclerosis exacerbations decreased in the 1980s as intravenous (IV) corticosteroid treatment became more common. Two RCTs published in the late 1980s compared ACTH with IV corticosteroids. A trial by Milanese et al (1989), which assessed 30 patients, found that dexamethasone was more effective than ACTH in shortening the length of the exacerbation.7 Thompson et al (1989) conducted a study that evaluated 61 patients and compared ACTH with high-dose IV methylprednisolone.8 The trialists did not find a statistically significant difference in the efficacy of the 2 treatments.

Case Series
There are also a limited number of small case series reporting on the use of ACTH for other corticosteroid-responsive conditions. For example, Gillis et al (2017) published a small case series of 8 adults with confirmed rheumatoid arthritis and American College of Radiology functional status between 1 and 3.9 Patients were refractory to prior therapies with at least 3 different modes of action. Repository corticotropin injection was administered for 12 weeks, with follow-up visits at weeks 14 and 16 (after cessation of repository corticotropin injection). Both physician and patient visual analog scale
assessments of swollen and tender joints improved from baseline to 12 weeks: physician visual analog scale scores significantly decreased from median of 8.4 (range, 3.8-9.9) to 2.5 (range, 0.30-6.5; p<0.001); patient visual analog scale scores decreased from median of 28.5 (range, 8-97) to 17 (range, 0-40; p=0.022). The 28-item Disease Activity Score for rheumatoid arthritis was also used as an outcome measure. As an open-label, unblinded study, there was potential for sampling bias, and patients were permitted to continue a variety of concomitant medication during repository corticotropin injection treatment.

Bomback et al (2011) published a retrospective case series in 21 patients with idiopathic, nondiabetic nephrotic syndrome who were treated with ACTH gel. ACTH gel was used as a primary therapy in 3 patients; the other 18 patients had failed a mean of 2.3 immunosuppressive regimens before using ACTH gel. An additional 5 patients who were treated for less than 6 months and were taken off therapy for lack of response were not included in the analysis. Four (19%) of the 21 patients were in complete remission, defined as stable or improved renal function with final proteinuria falling to less than 500 mg/d. An additional 7 (33%) of 21 patients had a partial remission (at least a 50% reduction in proteinuria and final proteinuria 500-3500 mg/d).

Section Summary: Corticosteroid-Responsive Conditions
There is insufficient evidence that ACTH gel is at least as effective as IV corticosteroids for the treatment of multiple sclerosis. One RCT found that corticosteroids were more effective and another found no significant difference in efficacy.

NON-CORTICOSTEROID-RESPONSIVE CONDITIONS

Clinical Context and Test Purpose
The purpose of repository corticotropin injection is to provide a treatment option that is an alternative to or an improvement on existing therapies in patients with non-corticosteroid-responsive conditions.

The question addressed in this evidence review is: Does the use of repository corticotropin injection to treat non-corticosteroid-responsive conditions improve the net health outcome?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is individuals with non-corticosteroid-responsive conditions. Proposed examples include tobacco cessation therapy, acute gout, and childhood epilepsy.

Interventions
The therapy being considered is repository corticotropin injection.

Comparators
The following therapy is currently being used to treat non-corticosteroid-responsive conditions: standard of care.

Outcomes
The general outcomes of interest are reductions in symptoms and improvements in disease status.
Timing
Treatment duration and follow-up of at least 6 months after repository corticotropin injection is necessary to monitor for changes in symptoms and disease status.

Setting
Patients with non-corticosteroid-responsive conditions are actively managed by primary care physicians and specialists in an outpatient setting.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Systematic Reviews
Repository corticotropin injection has been proposed for several off-label non-corticosteroid-responsive conditions, including tobacco cessation, acute gout, and childhood epilepsy. Controlled studies were identified only for treatment of acute gout. Janssens et al. (2008) published a Cochrane review that compared the efficacy and safety of systemic corticosteroids in the treatment of acute gout with placebo, nonsteroidal anti-inflammatory drugs, colchicine, other active drugs, other therapies including repository corticotropin injection, or no therapy. Three head-to-head trials were identified; one compared systemic corticosteroids with oral indomethacin and intramuscular ACTH. The quality of the 3 studies identified was graded as very low to moderate. None found clinically relevant differences between the systemic corticosteroids and the comparator drugs, and important safety problems attributable to the used corticosteroids were not reported. Reviewers concluded that “There is inconclusive evidence for the efficacy and effectiveness of systemic corticosteroids in the treatment of acute gout.”

Section Summary: Non-Corticosteroid-Responsive Conditions
There is a lack of controlled studies evaluating ACTH for treatment of non-corticosteroid-responsive conditions, with the exception of gout. A Cochrane review identified a single trial comparing ACTH and systemic corticosteroids; this trial did not report clinically relevant differences in outcomes.

DIAGNOSTIC TESTING OF ADRENOCORTICAL FUNCTION
Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.
Clinical Context and Test Purpose
The purpose of repository corticotropin injection in patients with suspected adrenocortical insufficiency is to inform a decision whether to proceed to treatment.

The question addressed in this evidence review is: Does the use of repository corticotropin injection for adrenocortical function testing improve the net health outcome?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is individuals who need a diagnostic assessment of adrenal function.

Interventions
The test being considered is repository corticotropin injection.

Comparators
The following test is currently being used to make decisions about diagnosing adrenal insufficiency: testing with the synthetic adrenocorticotropic hormone.

Outcomes
The general outcomes of interest are test validity and other test performance measures.

Timing
Laboratory testing of adrenocortical function is contemporaneous with the administration of the corticosteroid agent.

Setting
Patients requiring a diagnostic assessment of adrenal function are actively managed by endocrinologists and primary care providers in an outpatient setting.

Study Selection Criteria
For the evaluation of clinical validity of the repository corticotropin injection test, studies that met the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores)
- Included a suitable reference standard (describe the reference standard)
- Patient/sample clinical characteristics were described
- Patient/sample selection criteria were described.

Technically Reliable
Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist. This evidence review focuses on the clinical validity and clinical utility.

Clinically Valid
A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).
Studies have evaluated the value of synthetic ACTH for diagnosing adrenal insufficiency. For example, a meta-analysis by Kazlauskaite et al (2008) identified 13 studies comparing low- with high-dose corticotropin tests for diagnosing adrenal insufficiency. A comparable literature base was not identified for the use of natural ACTH (ie, H.P. Acthar gel used in the diagnostic testing of adrenocortical function), and no studies were found that compared synthetic with natural ACTH for this purpose.

**Clinically Useful**
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

**Direct Evidence**
Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No RCTs were identified assessing the clinical utility of the use of repository corticotropin injection in diagnosing adrenal insufficiency.

**Chain of Evidence**
Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the clinical validity of repository corticotropin injection testing in the diagnosis of adrenal insufficiency has not been established, a chain of evidence cannot be constructed.

**Section Summary: Diagnostic Testing of Adrenocortical Function**
No studies were identified that evaluated repository corticotropin injection, or compared natural with synthetic ACTH, for diagnostic assessment of adrenocortical function.

**SUMMARY OF EVIDENCE**
For individuals who have infantile spasms who receive repository corticotropin injection, the evidence includes randomized controlled trials, a systematic review, and a prospective cohort study. Relevant outcomes are symptoms and change in disease status. The systematic review judged the overall quality of the studies to be poor, with fewer than half reporting method of randomization and most assessing relatively few patients. There was heterogeneity across studies and either vigabatrin or prednisolone was used as comparators. Multivariate analysis of a prospective cohort study found that children with infantile spasms who were treated with ACTH were more likely to respond than other children. However, the analysis might have been subject to residual confounding on unmeasured characteristics; further, the study did not differentiate between synthetic and natural ACTH. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have corticosteroid-responsive conditions (eg, rheumatoid arthritis, dermatomyositis, sarcoidosis, nephrotic syndrome, multiple sclerosis, serum sickness) who receive repository corticotropin injection, the evidence includes randomized controlled trials and small case series. Relevant outcomes are symptoms and change in disease status. Overall, more recent studies evaluating multiple sclerosis have demonstrated that intravenous corticosteroids are at least as effective, or more effective, than repository corticotropin. Most studies assessing nephrotic syndrome have been small retrospective case studies. Ongoing studies are being conducted. The evidence is insufficient to determine the effects of the technology on health outcomes.
For individuals who have conditions not generally known to be responsive to corticosteroids (non-corticosteroid-responsive) such as tobacco cessation, childhood epilepsy, and acute gout who receive repository corticotropin injection, the evidence includes 3 head-to-head trials identified for use in gout. Relevant outcomes are symptoms and change in disease status. The quality of these studies was deemed very low to moderate because there were no direct placebo-controlled trials and no clinically relevant differences were detected between drugs studied. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who need diagnostic testing of adrenal function who receive repository corticotropin injection, the evidence does not include studies that compare the diagnostic accuracy of repository corticotropin injection with ACTH. Relevant outcomes are test validity and other test performance measures. The lack of published evidence precludes conclusions on the validity of using repository corticotropin as a diagnostic test for adrenal function. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

CLINICAL INPUT FROM PHYSICIAN SPECIALTY SOCIETIES AND ACADEMIC MEDICAL CENTERS
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 3 physician specialty societies and 1 academic medical center while this policy was under review in 2010. In addition, unsolicited input was received from 1 foundation and 3 physicians. There was strong support for use of repository corticotropin injection in the treatment of infantile spasms (West syndrome).

PRACTICE GUIDELINES AND POSITION STATEMENTS

American Academy of Neurology and Child Neurology Society
The American Academy of Neurology and the Child Neurology Society (2012) updated their evidence-based guidelines on the treatment of infantile spasms.13 The guidelines included the following recommendations on the use of adrenocorticotropic hormone (ACTH):

- “ACTH (Level B) or VGB [vigabatrin] (Level C) may be offered for short-term treatment of infantile spasms.”
- “Hormonal therapy (ACTH or prednisolone) may be considered for use in preference to VGB in infants with cryptogenic infantile spasms....”

Infantile Spasms Working Group
An industry-sponsored Infantile Spasms Working Group (2010) published a consensus report on the diagnosis and treatment of infantile spasms.14 Regarding treatment, the report concluded: “At this time, ACTH and VGB [vigabatrin] are the only drugs with proven efficacy to suppress clinical spasms and abolish the hypsarrhythmic EEG [electroencephalogram] in a randomized clinical trial setting (Mackay et al., 2004) and thus remain first-line treatment.”

American College of Rheumatology
The American College of Rheumatology (2012) published guidelines on therapy and anti-inflammatory prophylaxis of acute gouty arthritis.15 The guidelines committee did not reach a consensus on the use of ACTH for patients with acute gout who are able to take medications orally. For patients unable to take
oral medications, the committee agreed that subcutaneous synthetic ACTH was a reasonable alternative to oral prednisone or prednisolone therapy.

**U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS**
Not applicable.

**MEDICARE NATIONAL COVERAGE**
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

**ONGOING AND UNPUBLISHED CLINICAL TRIALS**
Some currently unpublished trials that might influence this review are listed in Table 2.

**Table 2. Summary of Key Trials**

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<th>Completion Date</th>
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<td>NCT02290444</td>
<td>Effects of Adrenocorticotropic Hormone (ACTHAR Gel) on Recovery From Cognitive Relapses in Multiple Sclerosis</td>
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<td>NCT02132195</td>
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<td>NCT02315872</td>
<td>The Effect of ACTH (Acthar) on Measures of Chronic Fatigue in Patients With Relapsing Multiple Sclerosis</td>
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<td>NCT01950234</td>
<td>Treatment of Progressive Forms of Multiple Sclerosis With Pulsed ACT (Acthar Gel)</td>
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<td><strong>Unpublished</strong></td>
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<td>NCT01386554</td>
<td>Acthar for Treatment of Proteinuria in Membranous Nephropathy Patients (CHART)</td>
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<td>NCT01601236</td>
<td>A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Adaptive Design Pilot Safety and Efficacy Study of H.P. Acthar Gel (Acthar) in Patients With Diabetic Nephropathy and Proteinuria</td>
<td>40</td>
<td>Mar 2016 (completed)</td>
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NCT: national clinical trial.
*a* Denotes industry-sponsored or cosponsored trial.

**REFERENCES**


**CODES**

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<td>Therapeutic, prophylactic or diagnostic injection (specify substance or drug); subcutaneous or intramuscular</td>
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<td>HCPCS</td>
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<td>Injection, corticotropin, up to 40 units</td>
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<td>Epileptic spasms code range (includes infantile spasms)</td>
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<td>ICD-10-PCS</td>
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<td>ICD-10-PCS codes are only used for inpatient services. There is no specific code for this procedure</td>
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**Type of service** Therapy

**Place of service** Inpatient

Home/outpatient

**POLICY HISTORY**

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**Original Policy Date:** February 2008
MP 5.01.17
Repository Corticotropin Injection

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<td>10/30/17</td>
<td>Replace policy</td>
<td>Blue Cross of Idaho adopted changes to policy as noted. Policy updated with literature review through August 28, 2017; no references added. Policy statements unchanged.</td>
</tr>
<tr>
<td>10/18/18</td>
<td>Replace policy</td>
<td>Blue Cross of Idaho adopted changes as noted, effective 10/18/2018. Policy updated with literature review through August 23, 2018; reference 9 added. Policy statements unchanged.</td>
</tr>
</tbody>
</table>