Repository Corticotropin Injection

Introduction

Corticotropin is a hormone made in certain cells in the pituitary gland. (Corticotropin may also be known as ACTH or adrenocorticotropin hormone.) When corticotropin is produced in a lab and used as a treatment, it’s believed that it helps the body create its own natural steroid hormones. Corticotropin injections may be approved to treat a rare seizure disorder that affects infants, known as West syndrome. Corticotropin injections have also been tried for several other conditions known to respond to steroid treatments. When medical studies compared corticotropin treatment with intravenous steroids, the studies did not show that the corticotropin treatments worked better. For this reason, corticotropin treatment is considered not medically necessary for conditions where steroids are a proven treatment. Corticotropin has also been tried for many other conditions including gout and childhood epilepsy. There isn’t enough high quality medical evidence to show whether it works. For this reason, corticotropin treatment is considered investigational (unproven) for many conditions.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.
### Policy Coverage Criteria

#### Drug | Medical Necessity
---|---
**Repository corticotropin injection*** | *Repository corticotropin* injection may be considered medically necessary for treatment of infantile spasms (West syndrome).

*Repository corticotropin injection may be considered not medically necessary in the following corticosteroid-responsive conditions, including, but not limited to:*

- Multiple sclerosis, acute exacerbation in adults
- Rheumatic disorders such as: psoriatic arthritis, rheumatoid arthritis, juvenile rheumatoid arthritis, ankylosing spondylitis
- Dermatologic diseases such as erythema multiforme, Stevens-Johnson syndrome
- Nephrotic syndrome – idiopathic or due to systemic lupus erythematosus (SLE)
- Ophthalmic diseases such as allergic and inflammatory processes of the eye: optic neuritis, keratitis, iritis, uveitis, choroiditis, chorioretinitis, anterior segment inflammation
- Respiratory diseases such as symptomatic sarcoidosis
- Allergic states such as serum sickness
- Collagen diseases such as systemic lupus erythematosus (SLE), systemic dermatomyositis (polymyositis)

*Repository corticotropin injection is considered not medically necessary for use in diagnostic testing of adrenocortical function.*

*Note: The brand name for repository corticotropin is H.P. Acthar Gel®*

#### Drug | Investigational
---|---
**Repository corticotropin injection** | *Repository corticotropin injection is considered investigational for conditions that are not responsive to corticosteroid therapy including, but not limited to:*
Drug | Investigational
---|---
| • Acute gout
| • Childhood epilepsy
| • Use in tobacco cessation

**Repository corticotropin injection is considered investigational for all other indications.**

### Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>CPT</strong>&lt;br&gt;96372</td>
<td>Therapeutic, prophylactic or diagnostic injection (specify substance or drug); subcutaneous or intramuscular</td>
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<tr>
<td><strong>HCPCS</strong>&lt;br&gt;J0800</td>
<td>Injection, corticotropin, up to 40 units</td>
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### Related Information

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

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.

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.

**Consideration of Age**

Any ages listed in the policy statements are based on FDA labeling.

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**Evidence Review**

**Description**

Repository corticotropin injection is a preparation of the natural form of adrenocorticotropic hormone (ACTH). The injection is used to treat corticosteroid-responsive conditions and as a diagnostic tool to test adrenal function.

**Background**

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.

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.

**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.

**Ongoing and Unpublished Clinical Trials**

Some currently unpublished trials that might influence this policy are listed in Table 1.
Table 1. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
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<tbody>
<tr>
<td><strong>Ongoing</strong></td>
<td></td>
<td></td>
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<tr>
<td>NCT02290444</td>
<td>Effects of Adrenocorticotropic Hormone (ACTHAR Gel) on Recovery From Cognitive Relapses in Multiple Sclerosis</td>
<td>60</td>
<td>Dec 2017 (ongoing)</td>
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<tr>
<td>NCT02132195</td>
<td>Adrenocorticotropic Hormone (ACTH) for Frequently Relapsing and Steroid Dependent Nephrotic Syndrome</td>
<td>60</td>
<td>Oct 2018</td>
</tr>
<tr>
<td>NCT02315872</td>
<td>The Effect of ACTH (Acthar) on Measures of Chronic Fatigue in Patients With Relapsing Multiple Sclerosis</td>
<td>8</td>
<td>Dec 2019</td>
</tr>
<tr>
<td>NCT01950234</td>
<td>Treatment of Progressive Forms of Multiple Sclerosis With Pulsed ACTH (Acthar Gel)</td>
<td>100</td>
<td>Mar 2022</td>
</tr>
<tr>
<td><strong>Unpublished</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>NCT01386554</td>
<td>Acthar for Treatment of Proteinuria in Membranous Nephropathy Patients (CHART)</td>
<td>60</td>
<td>May 2017 (completed)</td>
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<tr>
<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>
</tr>
</tbody>
</table>

NCT: national clinical trial

* Denotes industry-sponsored or cosponsored trial

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. The guidelines included the following recommendations regarding 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. 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. 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.

**Medicare National Coverage**

There is no national coverage determination.
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.

References


<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>02/09/16</td>
<td>New policy. Policy created to include plan specific medically necessary indications; replaces policy 5.01.17. Repository corticotropin injection may be considered medically necessary when criteria are met.</td>
</tr>
<tr>
<td>06/01/16</td>
<td>Interim Update, approved May 10, 2016. Language clarified regarding use the drug for steroid responsive conditions. FDA labeled conditions approved in 1952 were prior to the commercial availability of corticosteroid agents and not based on studies showing efficacy. Corticosteroid agents are available at lower cost and have stronger scientific evidence regarding their efficacy for most conditions, thus making this product not medically necessary based on contract language.</td>
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<tr>
<td>12/01/17</td>
<td>Annual Review, approved November 9, 2017. Policy updated with literature review through August 2017; no references added. Policy statements for corticosteroid-responsive conditions reorganized for clarity, including adding ophthalmic diseases.</td>
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<tr>
<td>09/21/18</td>
<td>Minor update. Added Consideration of Age statement.</td>
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