Repository Corticotropin

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**Related Coverage Resources**

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer’s particular benefit plan document (Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document) may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer’s benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer’s benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

**Coverage Policy**

Repository corticotropin (Acthar® Gel) is considered medically necessary when ALL of the following criteria are met:

- Individual is less than 2 years of age
- For the treatment of infantile myoclonic seizures
- Prescribed by, or in consultation with, a neurologist

Repository corticotropin (Acthar Gel) is considered not medically necessary for all other indications.

The effectiveness of repository corticotropin has not been demonstrated as clinically superior to conventional corticosteroids and/or immunosuppressive therapy (including prednisone and methylprednisolone) for uses other than infantile spasms. The alternatives (conventional corticosteroids and immunosuppressive therapies) are less costly. Coverage of repository corticotropin may depend on the applicable health benefit plan definition of medical necessity. Where that definition limits coverage to the most cost-effective equivalent treatment, repository corticotropin is not considered medically necessary.

Initial authorization is up to 1 month.
Repository corticotropin (Acthar Gel) is considered medically necessary for continued use when BOTH of the following criteria are met:

- Initial criteria are met
- Evidence of beneficial clinical response as submitted by the provider

Reauthorization is for up to 1 month.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Note: Receipt of sample product does not satisfy any criteria requirements for coverage.

**FDA Approved Indications**

**FDA Approved Indications**

**Infantile Spasms (IS)**
Acthar Gel is indicated as monotherapy for the treatment of IS in infants and children under 2 years of age.

**Multiple Sclerosis (MS)**
Acthar Gel is indicated for the treatment of acute exacerbations of MS in adults. Controlled clinical trials have shown Acthar Gel to be effective in speeding the resolution of acute exacerbations of MS. However, there is no evidence that it affects the ultimate outcome or natural history of the disease.

**Rheumatic Disorders**
As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in: psoriatic arthritis, rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy), ankylosing spondylitis.

**Collagen Diseases**
During an exacerbation or as maintenance therapy in selected cases of: systemic lupus erythematosus, systemic dermatomyositis (polymyositis).

**Dermatologic Diseases**
Severe erythema multiforme, Stevens-Johnson syndrome.

**Allergic States**
Serum sickness.

**Ophthalmic Diseases**
Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis; optic neuritis; chorioretinitis; anterior segment inflammation.

**Respiratory Diseases**
Symptomatic sarcoidosis.

**Edematous State**
To induce a diuresis or a remission of proteinuria in the nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus.
Recommended Dosing

FDA Recommended Dosing

Infantile Spasms (IS) in Infants and Children Under 2 Years of Age

In the treatment of IS, Acthar Gel must be administered intramuscularly. The recommended regimen is a daily dose of 150 U/m² (divided into twice daily intramuscular injections of 75 U/m²) administered over a 2-week period. Dosing with Acthar Gel should then be gradually tapered over a 2-week period to avoid adrenal insufficiency. The following is one suggested tapering schedule: 30 U/m² in the morning for 3 days; 15 U/m² in the morning for 3 days; and 10 U/m² every other morning for 6-days.

Acute Exacerbations in Adults with Multiple Sclerosis

The recommended dose is daily intramuscular or subcutaneous doses of 80 - 120 units for 2-3 weeks for acute exacerbations. Dosage should be individualized according to the medical condition of each patient. Frequency and dose of the drug should be determined by considering the severity of the disease and the initial response of the patient.

Other Indications for Adults and Children Over 2 Years of Age

Dosage should be individualized according to the disease under treatment and the general medical condition of each patient. Frequency and dose of the drug should be determined by considering severity of the disease and the initial response of the patient. The usual dose of Acthar Gel is 40-80 units given intramuscularly or subcutaneously every 24-72 hours.

Although drug dependence does not occur, sudden withdrawal of Acthar Gel after prolonged use may lead to adrenal insufficiency or recurrent symptoms which make it difficult to stop the treatment. It may be necessary to taper the dose and increase the injection interval to gradually discontinue the medication.

Drug Availability

Acthar Gel is supplied as a 5 mL multi-dose vial containing 80 USP Units per mL.

General Background

Current evidence does not support any definitive benefit to the use of Acthar Gel over conventional corticosteroids and/or immunosuppressive therapy (including prednisone and methylprednisolone) for FDA approved indications other than treatment of infantile myoclonic seizures. Acthar Gel is clinically equivalent but not superior to conventional corticosteroids and/or immunosuppressive therapy for the treatment of multiple sclerosis, rheumatic disorders, collagen diseases, dermatologic disorders, allergic states, ophthalmic diseases, respiratory diseases, or edematous states, and is significantly more expensive. Coverage for Acthar Gel may therefore depend upon the applicable health benefit plan definition of medical necessity. Where that definition limits coverage to the most cost-effective equivalent treatment, the use of Acthar Gel for indications other than infantile myoclonic seizures is considered not medically necessary.

Pharmacology

Acthar Gel is a natural form of adrenocorticotropic hormone (ACTH). Croticopein is not a corticosteroid. The mechanism of action of Acthar Gel in the treatment of infantile spasms is unknown. However, it shares many actions of the corticosteroids due to its ability to increase endogenous corticosteroid synthesis. It is rapidly absorbed following intramuscular administration, and the repository dosage form is slowly absorbed over approximately 8–16 hours.

Although repository corticotrophiin is FDA approved for the conditions listed above, it has limited therapeutic value in conditions responsive to corticosteroid therapy. In such cases, corticosteroids are considered the drugs of choice. Corticotrocipin therapy is not curative and generally suppresses the symptoms of chronic diseases without altering the natural course of the disease. It is considered to be supportive therapy to be used adjunctively with other indicated therapies. Generally, corticotrophiin therapy should be used for treatment only when disease is refractory to non-corticosteroid therapies.
Professional Societies/Organizations
American Academy of Neurology (AAN) and the Practice Committee of the Child Neurology Society
In June 2012, the AAN and the Practice Committee of the Child Neurology Society published new evidence-based guidelines and recommendations for medical treatment of infantile spasms. Sixty-eight articles dated from 2002 – 2011 were selected for detailed review - 26 were included in the analysis.

The results of the analysis determined there is insufficient evidence to determine whether other forms of corticosteroids are as effective as adrenocorticotropic hormone (ACTH) for short-term treatment of infantile spasms. However, low-dose ACTH is probably as effective as high-dose. ACTH is more effective than vigabatrin (VGB) for short-term treatment of children with infantile spasms (excluding those with tuberous sclerosis complex). There is insufficient evidence to show that other agents and combination therapy are effective for short-term treatment of infantile spasms. Short lag time to treatment leads to better long-term developmental outcome. Successful short-term treatment of cryptogenic infantile spasms with ACTH or prednisolone leads to better long-term developmental outcome than treatment with VGB.

The AAN and the Practice Committee of the Child Neurology Society recommend low-dose ACTH as a consideration for treatment of infantile spasms. ACTH or VGB may be useful for short-term treatment of infantile spasms, with ACTH considered preferential over VGB. Hormonal therapy (ACTH or prednisolone) may be considered for use in preference to VGB in infants with cryptogenic infantile spasms, to possibly improve developmental outcome. A shorter lag time to treatment of infantile spasms with either hormonal therapy or VGB possibly improves long-term developmental outcomes. (Go, 2012)

American College of Rheumatology (ACR)
In October 2012, the ACR published evidence-based guidelines and recommendations for the management of acute gouty arthritis. The guidelines state to treat an acute gouty arthritis attack with pharmacologic therapy and that treatment should be initiated within 24 hours of onset of an acute gout attack. The ACR recommend the use of oral nonsteroidal anti-inflammatory drugs (NSAIDs), oral and systemic corticosteroids, or oral colchicine and do not recommend one therapeutic class over another. (Khanna, 2012)

The American Board of Internal Medicine’s (ABIM) Foundation Choosing Wisely® Initiative:
No recommendations are available for repository corticotropin.

Centers for Medicare & Medicaid Services - National Coverage Determinations (NCDs)
There are no CMS National Coverage Determinations for repository corticotropin.

Clinical Efficacy
FDA Approved indications
The FDA label only provides clinical trial data on infantile spasms, no other uses. There is no FDA nor published data evaluating the safety and efficacy of repository corticotropin for the following uses: rheumatic disorders, collagen diseases, dermatologic diseases, allergic states, and ophthalmic diseases.

Infantile Spasms
The effectiveness of 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 Acthar Gel (75 U/m² 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 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 Acthar Gel treatment. Seven of 8 patients (87.5%) responded to
Acthar Gel after not responding to prednisone. Similarly, the 2 nonresponder patients from the 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 Acthar Gel.

Multiple Sclerosis Exacerbations
Few experimental randomized controlled trials have evaluated the efficacy of corticotropin for the treatment of acute exacerbations in patients with multiple sclerosis. Controlled studies evaluating the clinical efficacy of corticotropin in multiple sclerosis date back to 1961 with the most recent randomized controlled study published in 1989. It is unlikely that the corticotropin or ACTH products studied are identical to formulations available today. A Cochrane systematic review (Filippini G, 2000) includes 2 trials comparing corticotropin at various doses to placebo in multiple sclerosis patients who experienced an acute exacerbation of symptoms. Two additional trials compare the efficacy of corticotropin administered intramuscularly to intravenous methylprednisolone for the treatment of acute relapses in multiple sclerosis. Treatment of acute exacerbations with corticotropin significantly reduced the risk of worsening symptoms or no improvement better than placebo. Compared to methylprednisolone, one trial (Thompson, 1989) reported no significant differences in Kurtzke DSS scores or rates of improvement between corticotropin and methylprednisolone on days 3, 7, and 14, or at 1 and 3 months. Another trial (Barnes, 1985) reported no significant differences in Kurtzke DSS scores with corticotropin and methylprednisolone by day 7 and by 3 months but did find significant differences on day 3 and 28, favoring methylprednisolone.

Nephrotic Syndrome
A multicenter retrospective case series included 44 adult patients with Nephrotic Syndrome treated with Acthar gel at six clinics. The etiologies of Nephrotic Syndrome included the following: idiopathic focal segmental glomerulosclerosis (number of patients=15), idiopathic membranous nephropathy (11), IgA nephropathy (5), diabetic nephropathy (4), systemic lupus erythematosus class V membranous lupus nephritis (2), minimal change disease (2), membranoproliferative glomerulonephritis (1), fibrillary glomerulonephritis (1), and unbiopsied Nephrotic Syndrome (3). The response to proteinuria was evaluated assessed from baseline and the percent of patients meeting complete remission (defined as final proteinuria less than 500 mg/d), partial remission (defined as greater than or equal to 50% reduction in proteinuria from baseline and final proteinuria between the levels of 500 and 3500 mg/d), clinical response (defined as greater than or equal to 30% reduction in proteinuria from baseline that did not meet criteria for complete or partial remission), and no response (defined as failure to meet remission or clinical response per the criteria) following Acthar gel therapy. Results demonstrated that proteinuria reduction ≥30% was shown in 81.1% of patients and 62.2% showed ≥50% proteinuria reduction. (Madan, 2016). The Madan study was a retrospective case series with small numbers of patients per each indication listed. This area lacks well designed randomized, double blinded control studies to support use over alternatives available.

Chronic Pulmonary Sarcoidosis
A 24 week, single-blind prospective study, comparing two doses of repository corticotropin, was conducted in 16 individuals receiving prednisone for chronic pulmonary sarcoidosis. Trial participants were required to demonstrate a 5% decrease in FVC in the previous year. Patients received an 80 mg loading dose of repository corticotropin for 10 days and then randomized to receive either 40 or 80 units of repository corticotropin twice weekly. At week 24, improvements in diffusing capacity for carbon monoxide (DLCO), King’s Sarcoidosis Questionnaire health status and fatigue score, as well as, a decrease in prednisone requirements were observed. Less than 50% of the individuals started on the 80 unit dose, remained on an 80 unit dose at week 24. This small trial demonstrated a prednisone-sparing effect of repository corticotropin in chronic pulmonary sarcoidosis patients. Improvements were also observed in DLCO and patient reported outcome tests. The 40-unit dose was better tolerated and equally effective as the 80-unit dose. (Baughman, 2017)
Use in this indication lacks well designed randomized, double blinded control studies to support use over alternatives available.

Off Label Uses
AHFS Drug Information 2019 Edition does not support any off-label uses of Acthar.
Experimental, Investigational, Unproven Uses
There is no clinical trial data evaluating the safety and efficacy of repository corticotropin for the management of acute gouty arthritis.

Coding/ Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

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<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>J0800</td>
<td>Injection, corticotropin, up to 40 units</td>
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References


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