Repository Corticotropin Injections

Policy Number: 2025D0037U
Effective Date: October 1, 2025

➲ Instructions for Use

Table of Contents **Page**

Community Plan Policy

- Repository Corticotropin Injections

Coverage Rationale

➲ See Benefit Considerations

This policy refers to the following drug products:

- Acthar® Gel (repository corticotropin injection)
- Purified Cortrophin Gel™ (repository corticotropin injection USP)

Acthar Gel (repository corticotropin injection) and Purified Cortrophin Gel (repository corticotropin injection USP) are proven and medically necessary for the treatment of:

- **Infantile spasm** (i.e., West Syndrome) for up to 4 weeks when **all** of the following criteria are met:
  - Diagnosis of infantile spasms (i.e., West Syndrome); **and**
  - Patient is less than 2 years old; **and**
  - Provider attestation that the caregiver is not able to be trained or is physically unable to administer the drug; **and**
  - Provider must submit explanation; **and**
  - Dosing is in accordance with the United States Food and Drug Administration (FDA) approved labeling; **and**
  - Authorizations will be for no longer than 1 month
- **Opsoclonus-myoclonus syndrome** (i.e., Kinsbourne Syndrome) when **both** of the following criteria are met:
  - Diagnosis of opsoclonus-myoclonus syndrome (i.e., Kinsbourne Syndrome); **and**
  - Provider attestation that the caregiver is not able to be trained or is physically unable to administer the drug; provider must submit explanation; **and**
  - Authorizations will be for no longer than 3 months

Acthar Gel and Purified Cortrophin Gel are not medically necessary for treatment of acute exacerbations of multiple sclerosis. For non-medical necessity plans, Acthar Gel and Purified Cortrophin Gel may be covered for the treatment of acute exacerbation of multiple sclerosis (MS).

Acthar Gel and Purified Cortrophin Gel are unproven and not medically necessary for treatment of the following disorders and diseases:

- Allergic States: Serum sickness and atopic dermatitis
- Collagen Diseases: Systemic lupus erythematosus and systemic dermatomyositis (polymyositis)
- Dermatologic Diseases: Severe erythema multiforme, Stevens-Johnson syndrome, and severe psoriasis
- 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

- 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, and anterior segment inflammation
- Respiratory Diseases: Symptomatic sarcoidosis
- Rheumatic Disorders: Psoriatic arthritis, rheumatoid arthritis, including juvenile rheumatoid arthritis, ankylosing spondylitis, and acute gouty arthritis
- Any indication outside of the proven indications above

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J0801	Injection, corticotropin (Acthar Gel), up to 40 units
J0802	Injection, corticotropin (ANI), up to 40 units

Diagnosis Code	Description
G25.3	Myoclonus
G25.9	Extrapyramidal and movement disorder, unspecified
G35.A	Relapsing-remitting multiple sclerosis **(only for those members without medical necessity)**
G35.B0	Primary progressive multiple sclerosis, unspecified **(only for those members without medical necessity)**
G35.B1	Active primary progressive multiple sclerosis **(only for those members without medical necessity)**
G35.B2	Non-active primary progressive multiple sclerosis **(only for those members without medical necessity)**
G35.C0	Secondary progressive multiple sclerosis, unspecified **(only for those members without medical necessity)**
G35.C1	Active secondary progressive multiple sclerosis **(only for those members without medical necessity)**
G35.C2	Non-active secondary progressive multiple sclerosis **(only for those members without medical necessity)**
G35.D	Multiple sclerosis, unspecified **(only for those members without 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
H55.89	Other irregular eye movements

Background

Repository corticotropin is an adrenocorticotropic hormone (ACTH) analogue. Repository corticotropin and ACTH stimulate the adrenal cortex to secrete cortisol, corticosterone, aldosterone, and a number of weakly androgenic substances. Prolonged administration of large doses of repository corticotropin i induces hyperplasia and hypertrophy of the adrenal cortex and continuous high output of cortisol, corticosterone, and weak androgens. The release of endogenous ACTH is influenced by the nervous system via the regulatory hormone released from the hypothalamus and by a negative corticosteroid feedback mechanism. Elevated plasma cortisol suppresses ACTH release. Repository corticotropin also binds to melanocortin receptors. Both endogenous ACTH and repository corticotropin injection have a trophic effect on the adrenal cortex which is mediated by cyclic adenosine monophosphate (cyclic AMP).

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy.

Clinical Evidence

Proven

Infantile Spasms (i.e., West Syndrome)

In a prospective, randomized, single-blinded study, Baram et al compared the efficacy of corticotropin (ACTH) and prednisone in suppressing clinical spasms and hypsarrhythmic electroencephalogram (EEG) in infantile spasms. Patients were randomized to receive either a 2-week course of treatment with repository corticotropin injection (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 repository corticotropin 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 repository corticotropin treatment. Seven of 8 patients (87.5%) responded to repository corticotropin after not responding to prednisone. Similarly, the 2 nonresponder patients from the repository corticotropin treatment were eligible to receive treatment with prednisone. One of the 2 patients (50%) responded to the prednisone treatment after not responding to repository corticotropin.

In a single-center, single-blind, parallel-group, randomized clinical trial, Wanigasinghe et al compared the efficacy of ACTH and high-dose prednisolone for treatment of newly diagnosed West Syndrome (WS). Ninety-seven infants, newly diagnosed with WS, were randomized to receive either 14 days of oral prednisolone (40 to 60 mg/day) or an intramuscular (IM) injection of ACTH (40 to 60 IU/ every other day) according to the United Kingdom Infantile Spasm Study protocol. Patients were blindly evaluated for infantile spasm remission by day 14, including using a 30-minute electroencephalograph (EEG) as well as continued spasm freedom for 28 days. Forty-eight infants received prednisolone, and 49 infants received ACTH. By day 14, cessation of infantile spasms occurred in 58.3% of infants (28/48) on prednisolone, compared with only 36.7% (18/49) of infants given ACTH ($p = 0.03$). EEG and spasm cessation showed electroclinical remission in 21 prednisolone infants versus 9 ACTH infants ($p = 0.008$). Days required for spasm remission was significantly less in the prednisolone group (3.85 days ±2.4) compared with ACTH (8.65 days ±3.7) ($p = 0.001$).

Opsoclonus-Myoclonus Syndrome (i.e., OMS, Kinsbourne Syndrome)

Pranzatelli et al measured cerebrospinal fluid (CSF) ACTH and cortisol in 69 children with OMS and 25 age- and sex matched control subjects to determine endogenous levels and to look for hypothesized differential hormonal effects of ACTH and corticosteroid treatment. To compare high-dose versus low-dose, the ACTH-treated group was divided at the median (32 IU/m2/day) and the steroid group was also divided at the median (1.5 mg/kg/day). In cases of alternate day dosing, the dose was halved as an approximation for comparison with the daily dose group. CSF cortisol was 10-fold higher in the 26 patients receiving ACTH treatment ($p < 0.05$) but was unchanged with oral steroid treatment ($n = 18$) or no treatment ($n = 25$). It was significantly higher (25-fold) in children receiving daily high-dose ACTH than alternate day ACTH. In ACTH-treated children, CSF and serum cortisol were highly correlated ($p = 0.0001$), with a mean ratio of CSF to serum cortisol of approximately 1:10. CSF ACTH concentration did not differ significantly between untreated OMS and control subjects but was lower with ACTH (-29%) or steroid treatment (-36%), suggesting feedback inhibition of ACTH release ($p < 0.05$). Results indicated that daily high-dose ACTH treatment dramatically raises the concentration of CSF cortisol, but alternate day and low-dose ACTH did not.

Tate et al evaluated the efficacy and safety of corticotropin-based immunotherapies in a prospective, rater-blinded, exploratory study of previously untreated or steroid-dependent children ($n = 74$) with OMS. Children with neuroblastomas were excluded. Children were put into 1 of 6 groups: corticotropin alone or with intravenous immunoglobulin (groups 1 and 2, active controls); or both with rituximab (group 3) or cyclophosphamide (group 4); or with rituximab plus chemotherapy (group 5) or steroid sparers (group 6). Data was obtained through the Corticotropin Intake Form and Opsoclonus-Myoclonus Evaluation Scale. The primary end points were reduction in clinical severity relative to baseline (posttreatment total score and percentage improvement in total score). There was a 65% improvement in motor severity score across groups ($p < 0.0001$), but treatment combinations were more effective than corticotropin monotherapy ($p = 0.0009$). Groups

3, 4, and 5 responded better than group 1; groups 3 and 5 responded better than group 2. The response frequency to corticotropin was higher than to prior corticosteroids ($p < 0.0001$). Adverse events (corticosteroid excess) were reported in 55% of children, more so with multiagents ($p = 0.03$); and 10% of children ($n = 7$) had serious adverse events which were heterogeneous in etiology.

Unproven

The Acthar Gel and Purified Cortrophin Gel package inserts have listed other conditions in which they may be used without providing supporting clinical evidence. Since Acthar Gel and Purified Cortrophin Gel are more costly than alternatives that are at least as likely to produce equivalent therapeutic results, UHCP has determined that use of Acthar Gel and Purified Cortrophin Gel is unproven and not medically necessary for treatment of the following disorders and diseases:

- Rheumatic Disorders: psoriatic arthritis, rheumatoid arthritis, including juvenile rheumatoid arthritis, ankylosing spondylitis, and acute gouty arthritis.
- Collagen Diseases: systemic lupus erythematosus and systemic dermatomyositis (polymyositis).
- Dermatologic Diseases: Severe erythema multiforme, Stevens-Johnson syndrome, and severe psoriasis.
- Allergic States: Serum sickness and atopic dermatitis.
- 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, and 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.

Technology Assessments

Infantile Spasms (i.e., West Syndrome)

In 2010, the Infantile Spasms Working Group (ISWG) developed a consensus of the U.S. approach to the diagnostic evaluation and treatment of infantile spasms. There was strong consensus on the following four conclusions:

- The need for broad clinical evaluation, including detailed clinical neurophysiology was strongly recommended.
- ACTH and vigabatrin are the only drugs with proven effectiveness to suppress clinical spasms and abolish the hypsarrhythmic EEG (a specific EEG pattern found only in this syndrome) in a randomized clinical trial setting and thus remain first line treatments.
- Regardless of the chosen medication, timely assessment of treatment efficacy, i.e., two weeks for ACTH followed by taper (two weeks or less following dose titration for vigabatrin) and, if indicated, prompt treatment modification is strongly recommended as longer treatment trials, i.e., greater than two weeks for ACTH; greater than three months for vigabatrin are not likely to be effective and may come at the expense of serious adverse events.
- Effective treatment for infantile spasms should produce both cessation of spasms and resolution of hypsarrhythmia on EEG and is an all or none “response.”

In 2013, a Cochrane review was published comparing the effects of single drugs used to treat infantile spasms in terms of long-term psychomotor development, spasm control, subsequent epilepsy, and adverse effects. The following conclusions were made:

- To date, few well-designed randomized controlled trials have considered the treatment of infantile spasms, and the numbers of patients enrolled have been small.
- In the majority, methodology has been poor, hence it is not clear which treatment is optimal in the treatment of this epilepsy syndrome.
- Hormonal treatment resolves spasms in more infants than vigabatrin, but this may or may not translate into better long-term outcomes.
- If prednisolone or vigabatrin is used, high dosage is recommended.
- Vigabatrin may be the treatment of choice in tuberous sclerosis.
- Resolution of the EEG features may be important, but this has not been proven.
- Further research using large studies with robust methodology is required.

Multiple Sclerosis

In 2013, an update to the 2000 Cochrane review was published evaluating efficacy of corticosteroids ACTH versus no treatment (placebo) in reducing short- and long-term morbidity associated with multiple sclerosis (MS). The results of the review showed that that corticosteroids methylprednisolone (MP) or ACTH favored recovery from acute exacerbation in MS, increasing the probability of ameliorating the episode within the first five weeks of treatment by more than 60%. There was insufficient evidence to determine if steroids or ACTH treatment prevented new exacerbations and worsening of long-

term disability in MS. Evidence on the efficacy of different types or schedules of therapies was limited. Indirect comparisons suggest a significantly greater effect of MP versus ACTH.

In October 2014, The National Institute for Health and Care Excellences (NICE) published an updated clinical guideline entitled Management of Multiple Sclerosis (MS) in Primary and Secondary Care. In this publication, the Guideline Development Group (GDG) noted that some evidence for steroid use comes from older trials that had used ACTH, but that ACTH is no longer used as a treatment option for acute relapse of MS. The GDG considered that steroids are the common accepted treatment for relapse and that delivery is dependent on service organization. In June 2022, NICE published an updated clinical guideline entitled Management of Multiple Sclerosis in Adults: Management. Steroids remain the recommended treatment for acute relapses.

Professional Societies

In 2015, a Task Force of the International League Against Epilepsy (ILAE) Commission of Pediatrics developed a consensus document addressing diagnostic markers, management interventions, and outcome measures for infants with seizures. The task force concluded that for epileptic spasms, both high and low dose ACTH therapy is probably effective, and the task force strongly recommends.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Acthar Gel is an adrenocorticotropic hormone (ACTH) analogue indicated as monotherapy for the treatment of infantile spasms in infants and children less than 2 years of age and for the treatment of exacerbations of multiple sclerosis in adults. The FDA labeling suggests that Acthar Gel may be used for the following disorders and diseases: rheumatic; collagen; dermatologic; allergic states; ophthalmic; respiratory; and edematous states, however, it is not FDA indicated for these conditions.

Purified Cortrophin Gel is indicated in the following disorders and diseases: rheumatic; collagen; dermatologic; allergic states; ophthalmic; respiratory; edematous states, and nervous system.

References

1. Acthar Gel [package insert]. Bridgewater, NJ; Mallinckrodt ARD, LLC., February 2024.
2. Purified Cortrophin Gel [package insert]. Baudette, MN: ANI Pharmaceuticals, Inc.; December 2024.
3. Baram TZ, Mitchell WG, Tournay A, Snead OC, Hanson RA, Horton EJ. High-dose corticotropin (ACTH) versus prednisone for infantile spasms: a prospective, randomized, blinded study. *Pediatrics*. 1996;97(3):375-379.
4. Wanigasinghe J, Arambepola C, Sri Ranganathan S, Sumanasena S, Attanapola G. Randomized, Single-Blind, Parallel Clinical Trial on Efficacy of Oral Prednisolone Versus Intramuscular Corticotropin on Immediate and Continued Spasm Control in West Syndrome. *Pediatr Neurol*. 2015;53(3):193-199.
5. Shumiloff NA, Lam WM, Manasco KB. Adrenocorticotropic hormone for the treatment of West Syndrome in children. *Ann Pharmacother*. 2013;47(5):744-754.
6. Pranzatelli MR, Chun KY, Moxness M, Tate ED, Allison TJ. Cerebrospinal fluid ACTH and cortisol in opsoclonus-myoclonus: effect of therapy. *Pediatr Neurol*. 2005;33(2):121-126.
7. Tate ED, Pranzatelli MR, Verhulst SJ, et al. Active comparator-controlled, rater-blinded study of corticotropin-based immunotherapies for opsoclonus-myoclonus syndrome [published correction appears in J Child Neurol. 2012 Oct;27(10):1364. Dosage error in article text]. *J Child Neurol*. 2012;27(7):875-884.
8. Rose AS, Kuzma JW, Kurtzke JF, Namerow NS, Sibley WA, Tourtellotte WW. Cooperative study in the evaluation of therapy in multiple sclerosis. ACTH vs. placebo--final report. *Neurology*. 1970;20(5):1-59.
9. Abbruzzese G, Gandolfo C, Loeb C. "Bolus" methylprednisolone versus ACTH in the treatment of multiple sclerosis. *Ital J Neurol Sci*. 1983;4(2):169-172.
10. Barnes MP, Bateman DE, Cleland PG, et al. Intravenous methylprednisolone for multiple sclerosis in relapse. *J Neurol Neurosurg Psychiatry*. 1985;48(2):157-159.
11. Thompson AJ, Kennard C, Swash M, et al. Relative efficacy of intravenous methylprednisolone and ACTH in the treatment of acute relapse in MS. *Neurology*. 1989;39(7):969-971.

12. Simsarian JP, Saunders C, Smith DM. Five-day regimen of intramuscular or subcutaneous self-administered adrenocorticotropic hormone gel for acute exacerbations of multiple sclerosis: a prospective, randomized, open-label pilot trial. *Drug Des Devel Ther*. 2011;5:381-389.
13. Pellock JM, Hrachovy R, Shinnar S, et al. Infantile spasms: a U.S. consensus report. *Epilepsia*. 2010;51(10):2175-2189.
14. Hancock EC, Osborne JP, Edwards SW. Treatment of infantile spasms. *Cochrane Database Syst Rev*. 2013;2013(6):CD001770.
15. Filippini G, Brusaferri F, Sibley WA, et al. Corticosteroids or ACTH for acute exacerbations in multiple sclerosis. Cochrane Database Syst Rev. 2000;2000(4):CD001331.
16. National Clinical Guideline Centre (UK). *Multiple Sclerosis: Management of Multiple Sclerosis in Primary and Secondary Care*. London: National Institute for Health and Care Excellence (UK); October 2014.
17. *Multiple sclerosis in adults: management*. London: National Institute for Health and Care Excellence (NICE); June 22, 2022.
18. Wilmshurst JM, Gaillard WD, Vinayan KP, et al. Summary of recommendations for the management of infantile seizures: Task Force Report for the ILAE Commission of Pediatrics. *Epilepsia*. 2015;56(8):1185-1197.

Policy History/Revision Information

Date	Summary of Changes

10/01/2025	**Applicable Codes**
	• Updated list of applicable ICD-10 diagnosis codes to reflect annual edits:
	  ○ Added G35.A, G35.B0, G35.B1, G35.B2, G35.C0, G35.C1, G35.C2, and G35.D
	  ○ Removed G35
	Supporting Information
	• Archived previous policy version 2025D0037T

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.