

Clinical Policy: Repository Corticotropin Injection (Acthar Gel, Purified Cortrophin Gel)

Reference Number: HIM.PA.168

Effective Date: 06.01.23

Last Review Date: 05.24

Line of Business: HIM

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Repository corticotropin injection (Acthar[®] Gel, Purified Cortrophin[™] Gel) is adrenocorticotrophic hormone (ACTH) in gelatin.

FDA Approved Indication(s)

Acthar Gel is indicated as monotherapy for the treatment of infantile spasms in infants and children under 2 years of age.

Acthar Gel and Purified Cortrophin Gel are indicated for the treatment of acute exacerbations of multiple sclerosis (MS) in adults.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation[®] that Acthar Gel and Purified Cortrophin Gel are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. West Syndrome (Infantile Spasms) (must meet all):

1. Diagnosis of West syndrome (infantile spasms);
2. Request is for Acthar Gel;
3. Diagnosis is confirmed by electroencephalogram (EEG);
4. Prescribed by or in consultation with a neurologist;
5. Age < 2 years;
6. Dose does not exceed 150 U/m² per day (divided into twice daily injections of 75 U/m²).

Approval duration: 1 month

B. Multiple Sclerosis (must meet all):

1. Diagnosis of MS;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Prescribed for acute exacerbations of MS;

5. Failure of a recent (within the last 30 days) trial of at least a 7-day course of corticosteroid therapy for acute exacerbations of MS, unless contraindicated or clinically significant adverse effects are experienced;
 6. Member has not received treatment with Acthar Gel or Purified Cortrophin Gel for the current MS exacerbation;
 7. Member has been adherent to disease modifying therapy for MS (e.g., Aubagio[®], Avonex[®], Betaseron[®], Copaxone[®], Gilenya[®], Plegridy[®], Rebif[®]);
 8. For Purified Cortrophin Gel requests, member must use Acthar Gel, unless contraindicated or clinically significant adverse effects are experienced;
 9. Dose does not exceed 120 units (1.5 mL) per day and 6 vials total (*see Appendix D*).
- Approval duration: 3 weeks**

C. Nephrotic Syndrome (must meet all):

1. Diagnosis of nephrotic syndrome associated with one of the following (a - f):
 - a. Idiopathic membranous nephropathy (IMN);
 - b. Focal segmental glomerulosclerosis;
 - c. Minimal change disease (MCD);
 - d. Membranoproliferative glomerulonephritis;
 - e. Lupus nephritis;
 - f. IgA nephropathy;
2. Prescribed by or in consultation with a nephrologist;
3. Age > 2 years;
4. Failure of oral corticosteroid therapy, unless contraindicated or clinically significant adverse effects are experienced;
5. For IMN and MCD: Failure of cyclophosphamide, unless contraindicated or clinically significant adverse effects are experienced;
6. Failure of two of the following, unless clinically significant adverse effects are experienced or all are contraindicated: tacrolimus, cyclosporine, mycophenolate, rituximab;
7. For Purified Cortrophin Gel requests, member must use Acthar Gel, unless contraindicated or clinically significant adverse effects are experienced;
8. Dose does not exceed 80 units (1 mL) per day.

Approval duration: 3 months

D. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND

criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace.

II. Continued Therapy

A. West Syndrome (Infantile Spasms) (must meet all):

1. Member meets one of the following (a or b):
 - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
 - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Age < 2 years;
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed 150 U/m² per day (divided into twice daily injections of 75 U/m²).

Approval duration: 1 month (one renewal limit)

B. Multiple Sclerosis

1. Re-authorization is not permitted. Acthar is not indicated for continuous use for this indication. Members must meet the initial approval criteria.

Approval duration: Not applicable

C. Nephrotic Syndrome (must meet all):

1. Member meets one of the following (a or b):
 - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
 - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Member is responding positively to therapy;
3. For Purified Cortrophin Gel requests, member must use Acthar Gel, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, new dose does not exceed 80 units (1 mL) per day.

Approval duration: 3 months

D. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – HIM.PA.154 for health insurance marketplace or evidence of coverage documents;
- B.** The following conditions have not been proven in well-designed clinical trials and use is considered experimental:
 1. 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;
 2. Collagen diseases: During an exacerbation or as maintenance therapy in selected cases of: systemic lupus erythematosus; systemic dermatomyositis (polymyositis);
 3. Dermatologic diseases: severe erythema multiforme, Stevens-Johnson syndrome;
 4. Allergic states: serum sickness;
 5. 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;
 6. Respiratory diseases: symptomatic sarcoidosis.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

| | |
|-----------------------------------|--|
| ACTH: adrenocorticotropin hormone | IMN: idiopathic membranous nephropathy |
| EEG: electroencephalogram | MCD: minimal change disease |
| FDA: Food and Drug Administration | MS: multiple sclerosis |

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|-------------------------------------|
| tacrolimus (Prograf [®]) | Nephrotic syndrome: 0.05-0.075 mg/kg/day PO in two divided doses 12 hours apart | 0.075 mg/kg/day |
| cyclosporine (Neoral [®] , Sandimmune [®]) | Nephrotic syndrome: 3.5-5 mg/kg/day PO in two equally divided doses 12 hours apart | 5 mg/kg/day |
| cyclophosphamide | Nephrotic syndrome: 20 mg/kg/day PO for a 6-month course with alternating monthly cycles of PO and IV corticosteroids | 20 mg/kg/day |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|--|--|-----------------------------|
| mycophenolate (CellCept [®]) | Nephrotic syndrome: 2-3 g/day PO | 3 g/day |
| Rituxan [®] , Riabni [™] , Ruxience [™] , Truxima [®] (rituximab) | Nephrotic syndrome: 375 mg/m ² IV every week | 375 mg/m ² /week |
| methylprednisolone (Medrol [®] , Solu- Medrol [®]) | Acute exacerbation of multiple sclerosis: IM: 160 mg IM daily for 1 week, followed by 64 mg every other day for 1 month Oral: 160 mg PO per day for 1 week, followed by 64 mg every other day for 1 month | 160 mg/day |
| prednisone (Deltasone [®]) | Acute exacerbation of multiple sclerosis: 200 mg/day PO for 1 week, followed by 80 mg PO every other day for 1 month | 200 mg/day |
| dexamethasone (Decadron [®]) | Acute exacerbation of multiple sclerosis: 30 mg PO QD for 1 week followed by 4 to 12 mg PO every other day for 1 month | 30 mg/day |

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
 - Intravenous administration
 - Patients with 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;
 - Treatment of FDA approved indications accompanied by primary adrenocortical insufficiency or adrenocortical hyperfunction;
 - Acthar Gel Only:
 - Administration of live or live attenuated vaccines in patients receiving immunosuppressive doses of Acthar Gel;
 - Children under 2 years of age with suspected congenital infections;
- Boxed warning(s): none reported

Appendix D: General Information

- Common adverse reactions for Acthar Gel are similar to those of corticosteroids and include fluid retention, alteration in glucose tolerance, elevation in blood pressure, behavioral and mood changes, increased appetite and weight gain.
- The initial approval of Acthar Gel occurred prior to the Kefauver-Harris amendment to the Federal Food, Drug and Cosmetic Act of 1962, which introduced the requirement of “substantial evidence” of two adequate and well controlled trials. At the time of the original approval drug manufacturers only had to show the drug was safe for use in humans. The original data included case reports from a few physicians describing

patients with conditions originally treated with Acthar powder that were transferred to treatment with Acthar Gel and gave dosing guidance for treatment of these individual conditions.

- The efficacy Acthar Gel has in the following conditions has not been proven in well-designed clinical trials and its use is considered experimental.
 - 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
- Although Acthar Gel use in nephrotic syndrome has not been evaluated in well-designed clinical trials, it would be appropriate to allow use after exhausting alternative treatment options with higher quality of evidence to support their use that are supported by the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines for glomerulonephritis (e.g., corticosteroids, cyclophosphamide, cyclosporine, tacrolimus, mycophenolate, Rituxan).
- For acute exacerbations in multiple sclerosis, the results of trials that analyzed direct comparisons have shown no significant differences between ACTH and methylprednisolone (MP) in both rate and degree of recovery after exacerbation. Indirect comparisons suggest a significantly greater effect of MP versus ACTH, with MP conferring greater benefit compared with ACTH (odds ratio (OR) 0.20, 95% CI 0.09 to 0.45 vs OR 0.46, 95% CI 0.28 to 0.77).
- Studies evaluating the use of ACTH in acute exacerbations of multiple sclerosis ranged from 3 to 21 days in length and evaluated a reducing course of intramuscular ACTH over 14 days, consisting of 80 units for 7 days, 40 units for 4 days, and 20 units for 3 days. To date, retreatment with ACTH has not been evaluated in clinical trials.
- For acute exacerbation of multiple sclerosis, dosage and frequency should be individualized to the patient's needs, taking into account the patient's medical condition, severity of illness, and initial response to treatment. Prolonged use may lead to adrenal insufficiency or recurrent symptoms, which make it difficult to stop treatment. It may be necessary to taper the dose and gradually discontinue.

V. Dosage and Administration

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|------------------|----------------------------------|---|---------------------------|
| Acthar Gel | West syndrome (infantile spasms) | 150 U/m ² IM divided into twice daily injections of 75 U/m ² administered over a 2-week period. After 2 weeks, Acthar | 150 U/m ² /day |

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|-------------------------------------|--------------------------|--|---------------|
| | | Gel should be gradually tapered over a 2-week period | |
| Acthar Gel, Purified Cortrophin Gel | Acute exacerbation of MS | 80-120 units IM/SC daily for 2-3 weeks | 120 units/day |
| Acthar Gel, Purified Cortrophin Gel | Nephrotic syndrome | 40-80 units IM/SC every 24-72 hours | 80 units/day |

VI. Product Availability

| Drug Name | Availability |
|-------------------------|--|
| Acthar Gel | <ul style="list-style-type: none"> Multi-dose vial for IM or SC use: 5 mL containing 80 USP units/mL Pre-filled SelfJect injector for SC use: 40 USP units/0.5 mL, 80 USP units/mL |
| Purified Cortrophin Gel | Multi-dose vial: 1 mL, 5 mL containing 80 USP units/mL |

VII. References

1. Acthar Gel Prescribing Information. Hazelwood, MO: Mallinckrodt ARD, Inc.; February 2024. Available at: <https://www.acthar.com/>. Accessed March 11, 2024.
2. Purified Cortrophin Gel Prescribing Information. Baudette, MN: ANI Pharmaceuticals, Inc.; October 2023. Available at: www.cortrophin.com. Accessed January 29, 2024.
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14. Madan A, Mijovic-Das S, Stankovic A, et al. Acthar gel in the treatment of nephrotic syndrome: A multicenter retrospective case series. *BMC Nephrol.* March 31, 2016; 17:37.
15. Thompson AJ, Kennard C, Swash M, Summers B, Yuill GM, Shepherd DI, et al. Relative efficacy of intravenous methylprednisolone and ACTH in the treatment of acute relapse in MS. *Neurology* 1989;39(7):969–71.
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17. 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.
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Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPCS Codes | Description |
|-------------|---|
| J0801 | Injection, corticotropin (acthar gel), up to 40 units |
| J0802 | Injection, corticotropin (ani), up to 40 units |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|-----------------------------------|----------|-------------------|
| Policy created per April SDC. | 04.20.23 | 05.23 |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|--|----------|-------------------|
| In Appendix D, removed statement that H.P. Acthar Gel is not FDA approved in conditions lacking efficacy established with well-designed clinical trials. | 05.24.23 | |
| Added HCPCS codes [J0801, J0802] and deleted code [J0800]. | 10.27.23 | |
| 2Q 2024 annual review: for infantile spasm reduced approval durations from 3 to 1 month; for Purified Cortrophin Gel added 1 mL multiple dose vial formulation to Section VI; revised references to “H.P. Acthar Gel” to instead reference “Acthar Gel” per prescribing information; references reviewed and updated. RT4: for Acthar Gel updated product availability to include pre-filled injector. | 03.11.24 | 05.24 |

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible

CLINICAL POLICY
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for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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