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

Reference Number: PA.CP.PHAR.168
Effective Date: 01/2018
Last Review Date: 01/2024

Coding Implications
Revision Log

Description
Repository corticotropin injection (H.P. Acthar® Gel, Purified Cortrophin Gel) is adrenocorticotropic hormone (ACTH) in gelatin.

FDA Approved Indication(s)
H.P. Acthar Gel is indicated for the treatment of infantile spasms in infants and children under 2 years of age as monotherapy.

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

Policy/Criteria
It is the policy of PA Health & Wellness that H.P. Acthar Gel is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Infantile Spasms (must meet all):
1. Diagnosis of Infantile Spasms;
2. Request is for H.P. 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/m^2 per day (divided into twice daily injections of 75 U/m^2).

Approval duration: 1 month

B. Multiple Sclerosis (must meet all):
1. Diagnosis of multiple sclerosis (MS);
2. Age ≥ 18 years;
3. Prescribed by or in consultation with a neurologist;
4. Prescribed for acute exacerbations of MS;
5. Failure of a recent (within the last 30 days) trial of at least 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 H.P. 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®) or a clinical rationale must be provided for why the member is not using disease modifying therapy;

8. For H.P. Acthar Gel requests, member must use Purified Cortrophin Gel, if available, unless contraindicated or clinically significant adverse effects are experienced;
9. Dose does not exceed 120 units (1.5mL) 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 contraindicated or clinically significant adverse effects are experienced: tacrolimus, cyclosporine, mycophenolate, rituximab;
7. For H.P. Acthar Gel requests, member must use Purified Cortrophin Gel, if available, 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. Rheumatic Disorders, Collagen, Dermatologic, Ophthalmic, Respiratory Diseases, Allergic States (must meet all)**:**

1. Diagnosis of one of the following (a - f):
   a. Rheumatic disorder: 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, acute gouty arthritis;
   b. Collagen disease: During an exacerbation or as maintenance therapy in selected cases of: systemic lupus erythematosus; systemic dermatomyositis (polymyositis);
   c. Dermatologic disease: severe erythema multiforme, severe psoriasis, Stevens-Johnson syndrome;
   d. Ophthalmic disease: keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, allergic conjunctivitis, anterior segment inflammation;
   e. Respiratory diseases: symptomatic sarcoidosis;
   f. Allergic states: serum sickness, atopic dermatitis;
2. Prescribed by or in consultation with appropriate specialist;
3. Age > 2 years;

4. Trial and failure, contraindication or intolerance of ALL standard therapies for requested condition as recommended by consensus treatment guidelines;
5. Dose does not exceed 80 units (1 mL) per day.

Approval duration: 1 month

E. Other diagnoses/indications

1. Refer to PA.CP.PMN.53

II. Continued Approval

A. Infantile Spasms (must meet all):

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
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/m^2 (divided into twice daily injections of 75 U/m^2).

Approval duration: 1 month (one renewal limit)

B. Multiple Sclerosis:

1. HP Acthar is not indicated for continuous use for this indication. Reauthorization request must be reviewed against the initial approval criteria.

Approval duration: Not applicable

C. Nephrotic Syndrome (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. For H.P. Acthar Gel requests, member must use Purified Cortrophin Gel, if available, 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. Rheumatic Disorders, Collagen, Dermatologic, Ophthalmic, Respiratory Diseases, Allergic States (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Prescribed by or in consultation with appropriate specialist;
3. Age > 2 years;
4. Documentation indicating positive response to therapy;
5. Trial and failure, contraindication or intolerance of ALL standard therapies for requested condition as recommended by consensus treatment guidelines;
6. If request is for a dose increase, new dose does not exceed 80 units (1 mL) per day.

Approval duration: 3 months

E. Other Diagnoses/Indications (1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies
   Approval duration: Duration of request or 3 months (whichever is less); or
2. Refer to PA.CP.PMN.53

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 – PA.CP.PMN.53;

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ACTH: adrenocorticotropic hormone
EEG: electroencephalogram
FDA: Food and Drug Administration
IMN: idiopathic membranous nephropathy
MCD: minimal change disease
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
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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	200 mg/day PO for 1 week, followed by 80 mg PO every other day for 1 month	
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
  - H.P. Acthar Gel Only:
    - Administration of live or live attenuated vaccines in patients receiving immunosuppressive doses of H.P 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 H.P. 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 H.P. 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.
- Although H.P. 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
H.P. Acthar Gel	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, H.P. Acthar Gel should be gradually tapered over a 2-week period	150 U/m^2/day
H.P. Acthar Gel, Purified Cortrophin Gel	Acute exacerbation of MS	80-120 units IM/SC daily for 2-3 weeks	120 units/day
H.P. Acthar Gel, Purified Cortrophin Gel	Nephrotic syndrome	40-80 units IM/SC every 24-72 hours	80 units/day

VI. Product Availability

Multi-dose vial: 5 mL containing 80 USP units per mL

VII. References

1. H.P. Acthar Prescribing Information. Hazelwood, MO: Mallinckrodt ARD, Inc.; October 2021. Available at https://www.acthar.com/ . Accessed October 24, 2022.
2. Purified Cortrophin Gel Prescribing Information. Baudette, MN: ANI Pharmaceuticals, Inc.; November 2021. Available at: www.cortrophin.com. Accessed October 24, 2022.
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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
Removed indications not supported by well-designed clinical trials.West syndrome – removed EEG requirement to confirm diagnosis; added neurologist prescriber requirement. MS- approval duration reduced to one month for initial as this medication is not indicated to use chronically and for continued approval for MS was referred to the initial criteria. References reviewed and updated.	
1Q 2019 annual review: references reviewed and updated.	01/2019
1Q 2020 annual review: added mL quantity limits for multiple sclerosis and nephrotic syndrome indications; references reviewed and updated.	01/2020
Revised multiple sclerosis approval duration from 4 weeks to 3 weeks and added max vial quantity of 6 vials total; revised Appendix B and D; references reviewed and updated.	07/2020
1Q 2021 annual review: references reviewed and updated.	01/2021
Added experimental uses previously stated in Appendix D to Section III.	10/2021
1Q 2022 annual review: RT4: added Purified Cortrophin Gel to policy; for Acthar added step through Purified Cortrophin Gel per SDC; for infantile spasm added requirement that diagnosis is confirmed by EEG per competitor analysis; references reviewed and updated.	01/2022
1Q 2023 annual review: added the following for MS requests: Member has not received treatment with H.P. Acthar Gel or Purified Cortrophin Gel for the current MS exacerbation; updated HCPCS Codes to include J3490 for unclassified drugs as Purified Cortrophin Gel does not yet have a specific assigned HCPCS code; references reviewed and updated.	01/2023
1Q 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; updated HCPCS codes and revised to include J0801 and J0802; in Appendix D, removed statement that H.P. Acthar Gel is not FDA approved in conditions lacking efficacy established with well-designed clinical trials; references reviewed and updated.	01/2024