Prior Authorization Review Panel

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CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 11/01/2021**
Policy Number: PA.CP.PHAR.168	**Effective Date: 01/01/2018** **Revision Date: 10/2021**
Policy Name: Repository Corticotropin Injection (H.P. Acthar Gel)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

Added experimental uses previously stated in Appendix D to Section III.

Name of Authorized Individual (Please type or print): **Venkateswara R. Davuluri, MD**	**Signature of Authorized Individual:**

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

Reference Number: PA.CP.PHAR.168
Effective Date: 01/2018
Last Review Date: 10/2021

Coding Implications
Revision Log

Description
Repository corticotropin injection (H.P. Acthar® Gel) is adrenocorticotropic hormone (ACTH) in 16% 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
- Acute exacerbations of multiple sclerosis (MS) in adults.

Policy/Criteria
It is the policy of health plans affiliated with Pennsylvania Health and 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. Age < 2 years;
3. Prescribed by or in consultation with a neurologist;
4. Dose does not exceed 150 U/m^2 per day (divided into twice daily injections of 75 U/m^2).

Approval duration: 3 months

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 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;
7. Dose does not exceed 120 units (1.5mL) per day and 6 vials total (*see Appendix D*).

Approval duration: 1 months

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. Dose does not exceed 80 units (1 mL) per day.

Approval duration: 3 months

D. Other diagnoses/indications
1. Refer to PA.CP.PMN.53

II. Continued Approval

A. Infantile Spasms (must meet all):
1. Currently receiving medication via Pennsylvania Health and 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. Documentation indicating positive response 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: 3 months (one renewal limit)

B. Multiple Sclerosis: 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 Pennsylvania Health and 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. 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 (1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and 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;

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: adrenocorticotropic hormone
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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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® (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;
  - 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;
  - Treatment of FDA approved indications accompanied by primary adrenocortical insufficiency or adrenocortical hyperfunction
- 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.

- The efficacy HP Acthar Gel has in the following conditions has not been proven in well-designed clinical trials and its use is considered experimental. They are also not FDA approved indications:
  - 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 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

Indication	Dosing Regimen	Maximum Dose
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	150 U/m^2/day

Indication	Dosing Regimen	Maximum Dose
	Gel should be gradually tapered over a 2-week period	
Acute exacerbation of MS	80-120 units IM/SC daily for 2-3 weeks	120 units/day
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. VI. References

1. H.P. Acthar Prescribing Information. Hazelwood, MO: Mallinckrodt ARD, Inc.; March 2019. Available at https://www.acthar.com/ . Accessed November 4, 2020.
2. Go CY, Mackay MT, Weiss SK, et al. Evidenced-based guideline update: Medical treatment of infantile spasms: Report of the guideline development subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology.* June 12, 2012; 78(24): 1974-80. *Reaffirmed July 18, 2015.*
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11. Hogan J, Bomback AS, Mehta K, et al. Treatment of idiopathic FSGS with adrenocorticotropic hormone gel. *Clin J Am Soc Nephrol.* December 6, 2013; 8(12): 2072-2081.

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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
J0800	Injection, corticotropin, up to 40 units

Reviews, Revisions, and Approvals	Date	Approval 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.	01/19	
1Q 2020 annual review: added mL quantity limits for multiple sclerosis and nephrotic syndrome indications; references reviewed and updated.	01/20	
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.	07/20	
1Q 2021 annual review: references reviewed and updated.	01/21	

Reviews, Revisions, and Approvals	Date	Approval Date
Added experimental uses previously stated in Appendix D to Section III.	10/2021	