Clinical Policy Title:	repository corticotropin injection
Policy Number:	RxA.158
Drug(s) Applied:	H.P. Acthar® Gel
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Repository corticotropin injection (H.P. Acthar® Gel) is adrenocorticotropic hormone (ACTH) in 16% gelatin. It is indicated for the treatment of:

- Infantile spasms in infants and children under 2 years of age as monotherapy; and
- Acute exacerbations of multiple sclerosis (MS) in adults.

H.P. Acthar® Gel may be used for the following disorders/conditions:

- Rheumatic disorders for short-term administration (to tide the patient over an acute episode or exacerbation) in psoriatic arthritis, rheumatoid arthritis, juvenile rheumatoid arthritis, and ankylosing spondylitis;
- Collagen diseases during an exacerbation or as maintenance therapy in select cases of systemic lupus erythematosus, system dermatomyositis (polymyositis);
- Dermatologic disease (severe erythema multiforme and 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/chondroitis, optic neuritis, chorioretinitis, and anterior segment inflammation;
- Respiratory diseases (symptomatic sarcoidosis); and
- Edematous states to induce diuresis or remission of proteinuria in the nephrotic syndrome without uremia of idiopathic type or that is due to lupus erythematosus.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
repository corticotropin injection (H.P. Acthar® Gel)	West syndrome (infantile spasms)	150 units/m^2 IM divided into twice daily injections of 75 units/m^2 administered over a 2-week period. After 2 weeks, H.P. Acthar® Gel should be gradually tapered over a 2-week period and discontinued over a 2-week period.	150 units/m^2/day
	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
	Other conditions (see Appendix D)	40-80 units IM/SC every 24-72 hours	80 units/day

Dosage Forms

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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

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

1. Diagnosis of West syndrome (infantile spasms);
2. Prescribed by or in consultation with a neurologist;
3. Member is less than 2 years of age; and
4. Dose does not exceed 150 units/m^2 per day (divided into twice daily injections of 75 units/m^2).

Approval Duration
Commercial: 3 months
Medicaid: 3 months

B. Multiple Sclerosis (must meet all)**:**

1. Diagnosis of MS;
2. Prescribed by or in consultation with a neurologist;
3. Member is 18 years of age or older;
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®); and
7. Dose does not exceed 120 units per day.

Approval Duration
Commercial: 1 month
Medicaid: 1 month

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. Member is 2 years of age or older;
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 (2) of the following, unless contraindicated or clinically significant adverse effects are experienced: tacrolimus, cyclosporine, mycophenolate, rituximab; and
7. Dose does not exceed 80 units per day.

Approval Duration
Commercial: 3 months
Medicaid: 3 months

D. Other FDA Approved Indications (must meet all):
1. Member has one of the diagnoses or conditions listed in Appendix D;
2. Prescribed by or in consultation with an appropriate specialist based on the diagnosis;
3. Member is 2 years of age or older;
4. Failure of oral corticosteroid therapy, unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of other FDA approved agents (at least 2 if available) for the condition or the member has a contraindication to the agent; and
6. Dose does not exceed 80 units per day.

Approval Duration
Commercial: 3 months
Medicaid: 3 months

II. Continued Therapy Approval

A. West Syndrome (Infantile Spasms) (must meet all)**:**
1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is less than 2 years of age;
3. Member is responding positively to therapy; and
4. If request is for a dose increase, new dose does not exceed 150 units/m^2 per day (divided into twice daily injections of 75 units/m^2).

Approval Duration
Commercial: 3 months
Medicaid: 3 months

B. Multiple Sclerosis
1. Re-authorization is not permitted. H.P. Acthar® is not indicated for continuous use for this indication. Members must meet the initial approval criteria.

C. Nephrotic Syndrome (must meet all)**:**
1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy; and
3. If request is for a dose increase, new dose does not exceed 80 units per day.

Approval Duration
Commercial: 3 months
Medicaid: 3 months

D. Other FDA Approved Indications (must meet all)

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy; and
3. If request is for a dose increase, new dose does not exceed 80 units per day.

Approval Duration
Commercial: 3 months
Medicaid: 3 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
ACTH: Adrenocorticotropic hormone
FDA: Food and Drug Administration
IM: Intramuscular, intramuscularly
IMN: Idiopathic Membranous Nephropathy
MCD: Minimal Change Disease
MS: Multiple Sclerosis
PO: By mouth
SC: Subcutaneous, subcutaneously

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

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
rituximab (Rituxan®)	Nephrotic syndrome: 375 mg/m^2 IV every week	375 mg/m^2/week
vigabatrin (Sabril®, Vigadrone®)*	Infantile spasms: A typical dosing escalation scale of vigabatrin is an initial dose of 50 mg/kg per day, escalating to 100 to 150 mg/kg per day as required for clinical response.	200mg/kg/day
Glucocorticoids	Acute exacerbation of MS: Dosing varies based on product used. A preferred regimen of prednisone 1000 to 1250mg daily for 3-7 days without an oral taper is a preferred regimen.	Varies

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.
*Off-label

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

FDA Approved Indications Requiring Efficacy and Safety Documentation	
System	**Disease**
Rheumatic disorders	Psoriatic arthritis, rheumatoid arthritis, juvenile rheumatoid arthritis, ankylosing spondylitis
Collagen diseases	Systemic lupus erythematosus, systemic dermatomyositis (polymyositis)
Dermatologic diseases	Erythema multiforme, Stevens-Johnson syndrome
Allergic states	Serum sickness
Ophthalmic diseases	Keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, anterior segment inflammation
Respiratory diseases	Symptomatic sarcoidosis

- 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.

- 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 14 to 21 days in length and evaluated one course of therapy. To date, retreatment with ACTH has not been evaluated in clinical trials.

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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	1/2020	02/07/2020
Policy was reviewed: 1. Policy title table was updated. 2. Line of Business Policy Applies to was updated to all line of business. 3. Dosing information was updated to include Rheumatic disorders, Collagen diseases, Dermatologic diseases, Allergic states, Ophthalmic diseases, Respiratory diseases dosing regimen. 4. Initial and continued therapy approval was updated to include Medicaid approval duration. 5. "Other FDA Approved Indications" section was added to initial approval criteria and continued therapy. 6. Continued therapy criteria II.A.1. & II.C.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…" 7. Appendix D was updated with a chart including details about other FDA approved indications. 8. References were reviewed and updated.	07/1/2020	09/14/2020
Policy was reviewed: 1. Clinical Policy title was updated. 2. Criteria for other FDA approved indications updated. 3. Clinical policy - Verbiage added: ''The provision of provider samples does not guarantee coverage under the provisions of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage" after "Provider must submit…" 4. Continued Therapy criteria II.A.1, II.C.1, and II.D.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance..." 5. References were reviewed and updated.	02/25/2021	06/10/2021