

# REPOSITORY CORTICOTROPIN INJECTION (H.P. ACTHAR GEL®)

**Policy Number:** PHARMACY 214.16 T2

**Effective Date:** June 1, 2018

<b>Table of Contents</b>	<b>Page</b>
<a href="#">INSTRUCTIONS FOR USE</a> .....	1
<a href="#">CONDITIONS OF COVERAGE</a> .....	1
<a href="#">BENEFIT CONSIDERATIONS</a> .....	2
<a href="#">COVERAGE RATIONALE</a> .....	2
<a href="#">U.S. FOOD AND DRUG ADMINISTRATION</a> .....	3
<a href="#">BACKGROUND</a> .....	3
<a href="#">APPLICABLE CODES</a> .....	3
<a href="#">CLINICAL EVIDENCE</a> .....	3
<a href="#">REFERENCES</a> .....	6
<a href="#">POLICY HISTORY/REVISION INFORMATION</a> .....	7

<b>Related Policies</b>
<ul style="list-style-type: none"> <li>• <a href="#">Acquired Rare Disease Drug Therapy Exception Process</a></li> <li>• <a href="#">Drug Coverage Guidelines</a></li> <li>• <a href="#">Experimental/Investigational Treatment</a></li> <li>• <a href="#">Experimental/Investigational Treatment for NJ Plans</a></li> </ul>

## INSTRUCTIONS FOR USE

This Clinical Policy provides assistance in interpreting Oxford benefit plans. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage members. Oxford reserves the right, in its sole discretion, to modify its policies as necessary. This Clinical Policy is provided for informational purposes. It does not constitute medical advice. The term Oxford includes Oxford Health Plans, LLC and all of its subsidiaries as appropriate for these policies.

When deciding coverage, the member specific benefit plan document must be referenced. The terms of the member specific benefit plan document [e.g., Certificate of Coverage (COC), Schedule of Benefits (SOB), and/or Summary Plan Description (SPD)] may differ greatly from the standard benefit plan upon which this Clinical Policy is based. In the event of a conflict, the member specific benefit plan document supersedes this Clinical Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the member specific benefit plan coverage prior to use of this Clinical Policy. Other Policies may apply.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines 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.

## CONDITIONS OF COVERAGE

Applicable Lines of Business/ Products	This policy applies to Oxford Commercial plan membership.
Benefit Type	Medical <sup>2</sup>
Referral Required (Does not apply to non-gatekeeper products)	No
Authorization Required (Precertification always required for inpatient admission)	Yes <sup>1,2,3</sup>
Precertification with Medical Director Review Required	Yes <sup>2</sup>
Applicable Site(s) of Service (If site of service is not listed, Medical Director review is required)	Other
Special Considerations	<sup>1</sup> Providers must call Oxford's Pharmacy Benefit Manager (PBM) to obtain precertification for self-administration, covered under the pharmacy benefit. Refer to: <a href="#">Drug Coverage Guidelines</a> . <sup>2</sup> Precertification through Oxford's Medical Management

## BENEFIT CONSIDERATIONS

Before using this policy, please check the member specific benefit plan document and any federal or state mandates, if applicable.

- 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.
- Not all Oxford Members have pharmacy coverage. Refer to the member specific benefit plan document for additional information.
- For information regarding self-administration of H.P. Acthar Gel, refer to the policy titled [Drug Coverage Guidelines](#).
- For information regarding applicable quantity level limitations, refer to the policy titled [Drug Coverage Guidelines](#).
- Some Certificates of Coverage allow for coverage of experimental/investigational 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. Refer to the policies titled [Experimental/Investigational Treatment](#) and [Experimental/Investigational Treatment for NJ Plans](#).
- Benefit coverage for an otherwise not medically necessary service for the treatment of serious rare diseases may occur when certain conditions are met. Refer to the policy titled [Acquired Rare Disease Drug Therapy Exception Process](#).

### **Essential Health Benefits for Individual and Small Group**

For plan years beginning on or after January 1, 2014, the Affordable Care Act of 2010 (ACA) requires fully insured non-grandfathered individual and small group plans (inside and outside of Exchanges) to provide coverage for ten categories of Essential Health Benefits ("EHBs"). Large group plans (both self-funded and fully insured), and small group ASO plans, are not subject to the requirement to offer coverage for EHBs. However, if such plans choose to provide coverage for benefits which are deemed EHBs, the ACA requires all dollar limits on those benefits to be removed on all Grandfathered and Non-Grandfathered plans. The determination of which benefits constitute EHBs is made on a state by state basis. As such, when using this policy, it is important to refer to the member specific benefit plan document to determine benefit coverage.

## COVERAGE RATIONALE

### **H.P. Acthar Gel (repository corticotropin injection is proven and medically necessary for the treatment of:**

- **Infantile spasm (i.e., West Syndrome)<sup>1</sup> for up to 4 weeks when ALL of the following criteria are met:**
  - Diagnosis of infantile spasms (i.e., West Syndrome)<sup>1</sup>; **and**
  - Patient is less than 2 years old; **and**
  - Physician attestation that there is no competent caregiver to administer the drug. Physician must submit explanation; **and**
  - H.P Acthar Gel dosing for infantile spasm is as follows:
    - Initial dose: 75 U/m<sup>2</sup> intramuscular (IM) twice daily for 2 weeks
    - After 2 weeks, dose should be tapered according to the following schedule: 30 U/m<sup>2</sup> IM in the morning for 3 days; 15 U/m<sup>2</sup> IM in the morning for 3 days; 10 U/m<sup>2</sup> IM in the morning for 3 days; and 10 U/m<sup>2</sup> IM every other morning for 6 days (3 doses)
- **Opsoclonus-myooclonus syndrome (i.e., OMS, Kinsbourne Syndrome) when BOTH of the following criteria are met:**
  - Diagnosis of Opsoclonus-myooclonus syndrome (i.e., OMS, Kinsbourne Syndrome); **and**
  - Physician attestation that there is no competent caregiver to administer the drug. Physician must submit explanation.

### **H.P Acthar Gel is not medically necessary for treatment of acute exacerbations of multiple sclerosis.**

Published clinical evidence does not demonstrate superiority of Acthar to other available corticosteroids.

Although FDA labeling suggests that H.P. Acthar may be used in the following conditions, it is not FDA indicated.

### **H.P. Acthar 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

- Collagen diseases: 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
- 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
- Any indication outside of the medically necessary indications above

## U.S. FOOD AND DRUG ADMINISTRATION (FDA)

H.P. Acthar Gel is an adrenocorticotrophic 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 H.P. 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.<sup>1</sup>

## BACKGROUND

Repository corticotropin injection (H.P. Acthar Gel<sup>®</sup>) is an adrenocorticotrophic hormone (ACTH) analogue.<sup>1-3</sup> Repository corticotropin injection 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 injection 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 injection also binds to melanocortin receptor. Both endogenous ACTH and repository corticotropin injection have a trophic effect on the adrenal cortex which is mediated by cyclic adenosine monophosphate (cyclic AMP).

## 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 may apply.

HCPCS Code	Description
J0800	Injection, corticotropin, up to 40 units

ICD-10 Diagnosis Code	Description
G25.3	Myoclonus
G25.9	Extrapyramidal and movement disorder, unspecified
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

## CLINICAL EVIDENCE

### **Proven/Medically Necessary**

#### ***Infantile Spasms (i.e., West Syndrome)***

In a single-center, single-blind, parallel-group, randomized clinical trial, Wanigasinghe et al, investigated whether ACTH is not superior to 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). This followed the United Kingdom Infantile Spasm Study protocol. Infantile spasm (IS) remission was blindly evaluated 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  $\pm$  2.4) compared with ACTH (8.65 days  $\pm$  3.7) ( $P = 0.001$ ). The authors concluded that ACTH therapy at the trial dose did not yield superior rates of EEG or clinical remission when compared with the trial dose of prednisolone. More patients achieved electroclinical remission when treated with prednisolone than with ACTH.

### ***Opsoclonus-Myoclonus Syndrome (OMS, Kinsbourne Syndrome)***

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 opsoclonus-myoclonus syndrome (OMS).<sup>17</sup> 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 spacers (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). Researchers found that 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. Researchers concluded that the study demonstrated the greater efficacy of corticotropin-based multimodal therapy compared with conventional therapy and a greater response to corticotropin than corticosteroid-based therapy.

Cerebrospinal fluid (CSF) adrenocorticotrophic hormone (ACTH) concentration and cortisol were measured in 69 children with opsoclonus-myoclonus syndrome (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.<sup>16</sup> To compare high-dose versus low-dose, the ACTH-treated group was divided at the median (32 IU/m<sup>2</sup>/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. Researchers conclude that to the extent that cortisol is a factor in clinical response to ACTH therapy, data supports the use of high-dose ACTH protocols in OMS. Additionally, elevated brain cortisol may contribute to the superiority of ACTH treatment over oral corticosteroids in inducing a neurologic remission in OMS.

### **Unproven/Not Medically Necessary**

H.P. Acthar has additional uses listed in the FDA-label however, it is not FDA indicated. Since H.P. Acthar is more costly than an alternative drug that is at least as likely to produce equivalent therapeutic results, UHCP has determined that use of H.P. Acthar Gel is unproven and not medically necessary for treatment of the following disorders and diseases<sup>1,8-12,18-20</sup>

- **Rheumatic disorders:** psoriatic arthritis, rheumatoid arthritis, including juvenile rheumatoid arthritis, ankylosing spondylitis
- **Collagen diseases:** 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
- **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**

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 (Clinical Guideline 186).<sup>23</sup> 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 2013, an update to the 2000 Cochrane review was published evaluating efficacy and safety of corticosteroids or adrenocorticotropic hormone (ACTH) in reducing short and long term morbidity associated with multiple sclerosis (MS).<sup>14</sup> Authors conclude that:

- The trials evaluated showed that corticosteroids (methylprednisolone (MP)) or ACTH favored recovery from acute exacerbation in MS, which increased the probability of ameliorating the episode within the first five weeks of treatment by more than 60%. Evidence found that corticosteroids, notably MP, are effective in the treatment of acute exacerbation, increasing the probability of ameliorating the episode and speeding up patient recovery.
- 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 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.<sup>24</sup> Authors concluded that:

- 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.

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.<sup>15</sup> 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."

### **Professional Societies**

In 2015, a Task Force for the ILAE Commission of Pediatrics developed a consensus document addressing diagnostic markers, management interventions, and outcome measures for infants with seizures. For ACTH, the task force concluded that for epileptic spasms, both high and low dose ACTH therapy is probably effective and the task force strongly recommends.<sup>25</sup>

In the 2012, the American Academy of Neurology (AAN) updated their 2004 evidence-based guideline which summarizes the most effective therapies for infantile spasms, their safety, and whether successful treatment of infantile spasms leads to long-term improvement.<sup>13,21</sup> The recommendations of the AAN and Child Neurology Society (CNS) regarding medical treatment of infantile spasms in children is as follows for adrenocorticotropic hormone (ACTH)\*:

- The evidence is insufficient to recommend the use of prednisolone, dexamethasone, and methylprednisolone as being as effective as ACTH for short-term treatment of infantile spasms (Level U).
- Low-dose ACTH should be considered as an alternative to high-dose ACTH for treatment of infantile spasms (Level B).
- ACTH (Level B) or VGB (Level C) may be offered for short-term treatment of infantile spasms. Evidence suggests that ACTH may be offered over VGB (Level C).

- Hormonal therapy (ACTH or prednisolone) may be considered for use in preference to VGB in infants with cryptogenic infantile spasms, to possibly improve developmental outcome (Level C).
- A shorter lag time to treatment of infantile spasms with either hormonal therapy or VGB may be considered to improve long-term cognitive outcomes (Level C).

**\*AAN Rating of Recommendation:**

- Level A: Established as effective, ineffective or harmful for the given condition in the specified population.
- Level B: Probably effective, ineffective, or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population.
- Level C: Possibly effective, ineffective, or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population.
- Level U: Data inadequate or conflicting; given current knowledge, treatment is unproven.

## REFERENCES

The foregoing Oxford policy has been adapted from an existing UnitedHealthcare Pharmacy Clinical Pharmacy Program that was researched, developed and approved by the UnitedHealth Group National Pharmacy & Therapeutics Committee [2018D0037J]

1. H.P. Acthar Gel [prescribing information]. Hazelwood, MO . Mallinckrodt ARD, Inc., July 2017.
2. Gold Standard, Inc. Corticotropin, ACTH. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2016. Accessed April 7, 2018.
3. Corticotropin. In: DRUGDEX® [Internet database]. Greenwood Village, Colo: Truven Health Analytics, Inc.. Updated periodically. Accessed April 7, 2018.
4. Baram TZ, Mitchell WG, Tournay A, et al. High-dose corticotropin (ACTH) versus prednisone for infantile spasms: a prospective, randomized, blinded study. *Pediatrics* 1996;97:375-379.
5. FDA Acthar gel NDA 22-432 Peripheral and Central Nervous System Drugs Advisory Committee Meeting.. Accessed on April 7, 2018.
6. Hrachovy RA, Frost JD, Glaze DG et al. High-dose, long-duration versus low-dose, short duration corticotropin therapy for infantile spasms. *J Pediatr* 1994;124:803-806.
7. Kivity S, Lerman P, Ariel R, et al. Long-term cognitive outcomes of a cohort of children with cryptogenic infantile spasms treated with high-dose adrenocorticotrophic hormone. *Epilepsia*. 2004 Mar;45(3):255-62.
8. Simsarian JP, Saunders C and Smith DM. Five-day regimen of intramuscular or subcutaneous self-administered adrenocorticotrophic hormone gel for acute exacerbations of multiple sclerosis: a prospective, randomized, open-label pilot trial. *Drug Des Devel Ther*. 2011;5:381-9.
9. 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;39:969-971.
10. Barnes MP, Bateman DE, Cleland PG, et al. Intravenous methylprednisolone for multiple sclerosis in relapse. *J Neurol Neurosurg Psych*. 1985;48:157-159.
11. Abbruzzese G, Gandolfo C, Loeb C. "Bolus" methylprednisolone versus ACTH in the treatment of multiple sclerosis. *Ital J Neurol Sci*. 1983 Jun;4(2):169-72.
12. Rose AS, Kuzma JW, Kurtzke JF, et al. Cooperative study in the evaluation of therapy in multiple sclerosis: ACTH vs. placebo-final report. *Neurology*. 1970;20:1-59.
13. M. T. Mackay, S. K. Weiss, T. Adams-Webber, et al. Practice parameter: medical treatment of infantile spasms: report of the American Academy of Neurology and the Child Neurology Society. *Neurology* 2004;62:1668-81.
14. Filippini G, Brusafferri F, Sibley WA, Citterio A, Ciucci G, Midgard R, Candelise L. Corticosteroids or ACTH for acute exacerbations in multiple sclerosis. *Cochrane Database of Systematic Reviews* 2000, Issue 4. Art. No.: CD001331.
15. Pellock JM, Hrachovy R, Shinnar S, et al. Infantile spasms: a U.S. consensus report. *Epilepsia*. 2010 Oct;51(10):2175-89.
16. Pranzatelli M, Chun K, Moxness M, Tate E, Allison T. Cerebrospinal fluid ACTH and cortisol in opsoclonus-myoclonus: effect of therapy. *Pediatr Neurol*. 2005;33:121-126.
17. Tate ED, Pranzatelli MR, Verhulst SJ, et al. Active comparator-controlled, rater-blinded study of corticotropin-based immunotherapies for opsoclonus-myoclonus syndrome. *J Child Neurol*. 2012 Jul;27(7):875-84.
18. Bomback AS, Tumlin JA, Baranski J, Bourdeau, et al. Treatment of nephrotic syndrome with adrenocorticotrophic hormone (ACTH) gel. *Drug Des Devel Ther*. 2011;5:147-153.

19. Ponticelli C, Passerini P, Salvadori M, et al. A randomized pilot trial comparing methylprednisolone plus a cytotoxic agent versus synthetic adrenocorticotrophic hormone in idiopathic membranous nephropathy. *Am J Kidney Dis.* 2006 Feb;47(2):233-40.
20. Bomback A, Canetta P, Beck L, et al. Treatment of resistant glomerular diseases with adrenocorticotrophic hormone gel: a prospective trial. *Am J Nephrol.* 2012;36(1):58-67.
21. Go C, Mackay M, Weiss S, et al. Evidence-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.* 2012 Jun 12;78(24):1974-80.
22. National Clinical Guideline Centre. Multiple sclerosis: management of multiple sclerosis in primary and secondary care. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Oct. 36 p. (Clinical guideline; no. 186).
23. Wanigasinghe J, Arambepola C, Sri Ranganathan S, et al. 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 Sep;53(3):193-9.
24. Hancock EC, Osborne JP, Edwards SW. Treatment of infantile spasms. *Cochrane Database Syst Rev.* 2013; (6):CD001770.
25. 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 Aug;56(8):1185-97.

#### POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
06/01/2018	<ul style="list-style-type: none"> <li>• Updated supporting information to reflect the most current clinical evidence, FDA information, and references; no change to coverage rationale or lists of applicable codes</li> <li>• Archived previous policy version PHARMACY 214.15 T2</li> </ul>