Medical Drug Clinical Criteria

Subject:	Repository Corticotropin Injection		
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Overview

This document addresses the use of repository corticotropin injection agents. Acthar Gel and Cortrophin Gel are porcine derived purified corticotropin (ACTH) formulated in gelatin that can be administered via intramuscular or subcutaneous injection. Repository corticotropin is an adrenocorticotropic hormone analog that stimulates the adrenal cortex to secrete cortisol, corticosterone, aldosterone and a number of weakly androgenic substances. Product labeling states repository corticotropin injection may be used for the treatment of multiple sclerosis exacerbations and the following disorders and diseases: rheumatic, collagen, dermatologic, allergic states, ophthalmic, respiratory and edematous state. Acthar Gel has additional labeling for the treatment of infantile spasms.

Acthar Gel is approved by the Food and Drug Administration (FDA) as monotherapy for the treatment of infantile spasms in infants and children under 2 years of age. Infantile spasms is a rare and potentially life-threatening form of epilepsy that begins in the first year of life. It is characterized by a peculiar type of epileptic spasm along with electroencephalogram (EEG) findings of hypsarrhythmia and mental retardation. All three components are not required for diagnosis but when all three are present “West syndrome” is commonly used. The mechanism of action of repository corticotropin in the treatment of infantile spasms is unknown, but repository corticotropin can control spasms in individuals with adrenal suppression, signifying the mechanism is independent of the adrenal release of corticosteroids.

The efficacy of Acthar Gel for infantile spasms was established in a study by Baram and colleagues (1996) included in product labeling. In a single blinded clinical trial, children under 2 years of age with clinical spasms were randomized to receive either a 2-week course of treatment with Acthar (intramuscular injection twice daily) or prednisone (by mouth twice daily). The primary outcome was a comparison of the number of children in each group who were treatment responders (defined as having complete suppression of both clinical spasms and hypsarrhythmia on a full sleep cycle video electroencephalogram [EEG] performed 2 weeks following initiation of treatment). Of 15 infants randomized to Acthar, 13 (86.7%) responded as compared to 4 of 14 subjects (28.6%) given prednisone.

In 2012, the American Academy of Neurology (AAN) and the Practice Committee of the Child Neurology Society analyzed pre-2002 and more recent evidence on infantile spasms and subsequently revised their corresponding practice parameters. Recommendations include consideration of low-dose repository corticotropin injection for treatment of infantile spasms. The guidance also states repository corticotropin injection or vigabatrin may be useful for short-term treatment of infantile spasms with repository corticotropin injection considered preferentially over vigabatrin. The AAN reaffirmed this guidance in 2018 and 2021.

Product labeling states repository corticotropin injection is indicated for the treatment of exacerbations of multiple sclerosis in adults. Acute exacerbations of multiple sclerosis are typically steroid responsive and treated with corticosteroids such as methylprednisolone. Repository corticotropin injection augments circulating steroids via adrenal gland stimulation and therefore produces the same types of effects and side effects which occur when steroids are used. Exogenous corticosteroids are available in multiple formulations and delivery methods (oral, intravenous, intramuscular, subcutaneous) and are widely accepted as the appropriate therapy for steroid responsive conditions. Accordingly, there is no clinical basis for selecting repository corticotropin when an individual is able to receive exogenous corticosteroids.

Peer reviewed literature describing the use of repository corticotropin injection for the treatment of multiple sclerosis exacerbations consists mainly of old studies which are not of high quality (Miller, 1961; Rose, 1970; Thompson, 1989). Abbruzzese (1983) indicated there was equal efficacy for bolus methylprednisolone and repository corticotropin for the treatment of multiple sclerosis. In a systematic review, Filippini and colleagues (2000) examined the efficacy and safety of corticosteroids (methylprednisolone) and repository corticotropin in treating individuals with multiple sclerosis exacerbations. The authors noted that overall, methylprednisolone or repository corticotropin showed a protective effect against the disease getting worse or stable within the first 5 weeks of treatment (odds ratio 0.37, 95% confidence interval, 0.24 to 0.57). There was insufficient evidence to show whether either treatment prevented new exacerbations or worsening of long-term disability. Indirect comparisons suggest a significantly greater effect of methylprednisolone versus repository corticotropin.

Repository corticotropin injection has been used as an aid in the diagnosis of adrenocortical insufficiency; however, this indication was removed from the product label in October 2010. There is a lack of peer reviewed published literature to support this use.

In addition to infantile spasms and multiple sclerosis exacerbations, product labeling states repository corticotropin injection may be used for treatment of the following disorders and diseases: rheumatic, collagen, dermatologic, allergic states, ophthalmic, respiratory and edematous state. The published evidence in support of these conditions is limited.

A systemic review and meta-analysis of 36 clinical trials evaluated treatment for membranous nephropathy (Chen, 2013). Two studies (n=62) evaluated repository corticotropin and found significantly decreased proteinuria at the end of 22 months of follow-up. However, multiple study limitations were present including small sample sizes and a high risk of bias. There have been additional small studies and case series published evaluating repository corticotropin for a variety of conditions, including chronic pulmonary sarcoidosis (Baughman, 2017), systemic lupus erythematosus (Fiechtner, 2014), nephrotic syndrome (Bomback, 2011; Hladunewich, 2014; Madan, 2016); and membranous glomerulopathy (Watson, 2013). All authors concluded that repository corticotropin injection may be an effective therapy for their respective conditions. However, limitations included small numbers of participants.

In summary, there is moderate level of evidence in the peer reviewed literature for the use of repository corticotropin injection in the treatment of infantile spasms and only low quality evidence for its use in other conditions. Most of the studies for other conditions are case series or retrospective observation studies with significant limitations including non-blinding and very small sample size. Larger, randomized control trials are needed to support the use of repository corticotropin injection for the treatment of conditions other than infantile spasms. Given the lack of placebo-controlled trials to determine the optimal dose, duration of treatment and its role compared with corticosteroid therapy, repository corticotropin injection cannot be recommended for uses other than infantile spasms at this juncture.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Repository Corticotropin Injection (Acthar Gel, Purified Cortrophin Gel)

Requests for repository corticotropin injection (Acthar Gel, Purified Cortrophin Gel) may be approved if the following criteria are met:

I. Individual is an infant or child less than 2 years of age and is using as monotherapy for the treatment of infantile spasms (West syndrome).

Approval duration: 3 months

Repository corticotropin injection (Acthar Gel, Cortrophin Gel) may not be approved when the above criteria are not met and for all other indications.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J0801	Injection, corticotropin [Acthar Gel], up to 40 units
J0802	Injection, corticotropin [ANI], up to 40 units

ICD-10 Diagnosis

G40.821-G40.824	West Syndrome

Document History

Reviewed: 11/15/2024
Document History:

- 11/15/2024 – Annual Review: No changes. Coding Reviewed: Deleted HCPCS J0800.
- 11/17/2023 – Annual Review: No changes. Coding Reviewed: No changes. 08/19/2022 – Annual Review: Wording and formatting changes. Coding reviewed: No changes. Effective 10/1/2023 Added HCPCS J0801, J0802. Removed HCPCS J3490, J3590. Removed H.P. Acthar from J0800.
- 12/13/2021 – Select Review: Revise document name to include all repository corticotropin agents. Add Purified Cortrophin Gel to clinical criteria. Coding Reviewed: Removed ICD-10-CM G40.409-G40.419, Added HCPCS J3490, J3590.
- 8/20/2021 – Annual Review: No changes. Coding reviewed: No changes.
- 8/21/2020 – Annual Review: No changes. Coding reviewed: No changes.
- 12/9/2019 – Select Review: Clarify approval duration in Acthar criteria. Coding reviewed: Added G40.409-G40.419 West Syndrome.

- 8/16/2019 – Annual Review: Wording and formatting changes. Coding Reviewed: No changes.
- 11/9/2018 – Coding Review: Took out 'All Diagnosis' in coding and specified infantile spasms only.
- 8/17/2018 – Annual Review: Initial P&T review of ING-CC-0004 H.P. Acthar Gel (repository corticotropin injection). Limit approval criteria to infantile spasms.

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