PHARMACY COVERAGE GUIDELINE

ACTHAR® GEL (repository corticotropin) injection
PURIFIED CORTROPHIN™ GEL (repository corticotropin) injection
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

ACTHAR GEL (repository corticotropin)

- **Criteria for initial therapy:** Acthar Gel (repository corticotropin) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Neurologist

  2. Individual has a confirmed diagnosis of **ONE** of the following:
     a. Individual under 2 years of age with infantile spasms (also known as infantile epileptic spasms syndrome (IESS)) without tuberous sclerosis

b. Individual 18 years of age or older with acute exacerbation of multiple sclerosis (MS) who is adherent with maintenance immune suppressing agent for MS **AND** has failed, contraindication per FDA label, or intolerance to corticosteroids which are **not** expected to occur with use of Acthar Gel **AND** will not be using Acthar Gel monthly for prophylaxis of acute exacerbations of MS

c. Individual is 18 years of age or older with a corticosteroid responsive condition who has failure (after at least 6 months of use), contraindication per FDA label, or intolerance to corticosteroids which are **not** expected to occur with use of Acthar Gel

3. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

4. There are **NO** FDA-label contraindications such as:
   a. Intravenous administration
   b. Congenital infection suspected in an infant less than 2 years of age
   c. Administration of live or attenuated vaccines in an individual on immunosuppressive doses of Acthar Gel
   d. Scleroderma, osteoporosis, systemic fungal infections, ocular herpes simplex, recent surgery, history of or the presence of a peptic ulcer, congestive heart failure, uncontrolled hypertension, primary adrenocortical insufficiency, adrenocortical hyperfunction, or sensitivity to proteins of porcine origin

Initial approval duration: 4 weeks
Requests beyond 4 weeks requires a Medical Director review
Maximum of 35 mL (7 vials) will be authorized, requests for more vials requires a Medical Director review
- Acthar Gel vial is intended for either intramuscular or subcutaneous injection
- Acthar Gel single-dose pre-filled SelfJect injector is only for subcutaneous administration by adults (18 years of age and older) for administration of either 40 units or 80 units
- For administration of doses other than 40 units or 80 units, use the Acthar Gel multi-dose vial
- In the treatment of infantile spasms, Acthar Gel must be administered intramuscularly using the Acthar gel vial. Do not use the Acthar Gel single-dose pre-filled SelfJect injector for the treatment of infantile spasms

➢ **Criteria for continuation of coverage (renewal request):** Acthar Gel (repository corticotropin) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Neurologist

2. All requests for renewal or continuation will be reviewed using the above initial criteria and if approved the same duration will apply

3. Individual has been adherent with the medication

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follows:
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Infection including viral, bacterial, fungal, protozoan or helminthic infections
        ii. Adrenal insufficiency
        iii. Cushing's syndrome
        iv. Gastrointestinal perforation and bleeding
        v. Behavioral and mood disturbances such as severe depression, frank psychosis, others

Renewal duration: 4 weeks
Requests beyond 4 weeks requires a Medical Director review
Maximum of 35 mL (7 vials) will be authorized, requests for more vials requires a Medical Director review

- Acthar Gel vial is intended for either intramuscular or subcutaneous injection
- Acthar Gel single-dose pre-filled SelfJect injector is only for subcutaneous administration by adults (18 years of age and older) for administration of either 40 units or 80 units
- For administration of doses other than 40 units or 80 units, use the Acthar Gel multi-dose vial
- In the treatment of infantile spasms, Acthar Gel must be administered intramuscularly using the Acthar gel vial. Do not use the Acthar Gel single-dose pre-filled SelfJect injector for the treatment of infantile spasms

➢ Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

PURIFIED CORTROPHIN GEL (repository corticotropin)

➢ **Criteria for initial therapy:** Purified Cortrophin Gel (repository corticotropin) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Neurologist

2. Individual 18 years of age or older

3. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Acute exacerbation of multiple sclerosis (MS) in an individual who is adherent with maintenance immune suppressing agent for MS **AND** has failed, contraindication per FDA label or intolerance to corticosteroids which are **not** expected to occur with use of Purified Cortrophin Gel **AND** will not be using Purified Cortrophin Gel monthly for prophylaxis of acute exacerbations of multiple sclerosis

    b. Corticosteroid responsive condition in an individual who has failure (after at least 6 months of use), contraindication per FDA label or intolerance to corticosteroids which are **not** expected to occur with use of Purified Cortrophin Gel

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. There are **NO** FDA-label contraindications such as:
    a. Intravenous administration
    b. Scleroderma, osteoporosis, systemic fungal infections, ocular herpes simplex, recent surgery, history of or the presence of a peptic ulcer, congestive heart failure, hypertension, or sensitivity to proteins of porcine origin
    c. Primary adrenocortical insufficiency or adrenocortical hyperfunction

Initial approval duration: 4 weeks
Requests beyond 4 weeks requires a Medical Director review
Maximum of 35 mL (7 vials) will be authorized, requests for more vials requires a Medical Director review

- **Criteria for continuation of coverage (renewal request):** Purified Cortrophin Gel (repository corticotropin) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Neurologist

2. All requests for renewal or continuation will be reviewed using the above initial criteria and if approved the same duration will apply

3. Individual has been adherent with the medication

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follows:
    a. Contraindications as listed in the criteria for initial therapy section

b. Significant adverse effect such as:
   i. Infection
   ii. Adrenal insufficiency
   iii. Cushing's syndrome
   iv. Gastrointestinal perforation and bleeding
   v. Behavioral and mood disturbances such as severe depression, frank psychosis, others

Renewal duration: 4 weeks

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Repository corticotropin (Acthar Gel, Purified Cortrophin Gel) injection is a preparation of the natural form of adrenocorticotropic hormone (ACTH) in gelatin to provide a prolonged release after intramuscular or subcutaneous injection. ACTH works by stimulating the adrenal cortex to produce cortisol, corticosterone and a number of other hormones. Repository corticotropin is primarily used for treating infantile spasms, it has been investigated for diagnostic testing of adrenocortical function, and it has been used in the treatment of a variety of other conditions.

Repository corticotropin, as Acthar gel, was approved by the U.S. Food and Drug Administration (FDA) in 1952, before there was a requirement that innovator companies provide clinical evidence of efficacy of their product.

Prescription products have a package label that covers important information to guide prescribers on the proper use of the product such as product description, use, available dosage forms, dosing information, administration, contraindications, warnings/precautions, adverse effects, and other safety and efficacy data. The Clinical Studies section of the product label contains a brief review of the clinical study or studies that were presented to the FDA to obtain formal FDA approval.

Acthar Gel product label says that it is indicated for *infantile spasms* and indicated for the treatment of *acute exacerbations of multiple sclerosis*. The label lists several conditions where it says Acthar Gel may be used**.** The product label provides specific dosing and administration information for infantile spasms and acute exacerbations of multiple sclerosis and a usual dosage range and frequency for the other uses. The product label states that controlled clinical trials have shown ACTH to be effective in speeding the resolution of acute exacerbations of multiple sclerosis but there is no evidence that it affects the ultimate outcome or natural history of the disease. The clinical studies section of the product labeling of Acthar Gel describes efficacy data *only* for infantile spasms. Clinical efficacy and safety data for other uses are lacking. There is little data available for the listed general uses for rheumatic, collagen, dermatologic, allergic states, ophthalmic, respiratory, and edematous disorders/diseases.

These uses were grandfathered in by the FDA. Based on the lack of both efficacy and safety data for the above referenced grandfathered uses, these additional disorders will be considered unsupported.

Purified Cortrophin Gel product label says it is indicated for conditions where Acthar Gel stated it may be used. The product label also lists other conditions that are not included in Acthar Gel labelling. Purified Cortrophin Gel product label does not have a Clinical Studies section that would provide a summary of the data supporting use for these conditions. The label does not list infantile spasms as a use for the product. The product label provides specific dosing *only* for acute exacerbations of multiple sclerosis. Under the Precautions – General section it states that controlled clinical trials have shown ACTH to be effective in speeding the resolution of acute exacerbations of multiple sclerosis but there is no evidence that it affects the ultimate outcome or natural history of the disease. The label goes on to recommend a specific dose for acute exacerbations. Given the lack of both efficacy and safety data, use of Purified Cortrophin for other disorders will be considered unsupported except for acute exacerbations of multiple sclerosis.

Although repository corticotropin (Acthar Gel, Purified Cortrophin Gel) can be used to treat various other medical conditions responsive to corticosteroid therapy, it has not been proven to be superior to corticosteroids for these uses. Corticosteroid therapy is generally considered the treatment of choice. Acthar Gel and Purified Cortrophin have limited therapeutic value since they cannot be administered orally, and their effectiveness is dependent on adrenocortical responsiveness. There is a lack of controlled studies on repository corticotropin for treatment of non-corticosteroid-responsive conditions. The adverse effects of both Acthar Gel and Purified Cortrophin Gel are related primarily to steroid-like effects.

Acthar Gel is a naturally sourced complex mixture of adrenocorticotropic hormone analogs and other pituitary peptides. The manufacturing process converts the initial porcine pituitary extract with low ACTH content into a mixture having modified porcine ACTH and other related peptide analogs solubilized in gelatin. A major component in the formulated complex mixture is N-25 deamidated porcine ACTH (1-39). Acthar Gel is available as a 5 mL vial (80 units/mL, total of 400 units).

Purified Cortrophin Gel is a porcine derived purified corticotropin (ACTH) in a sterile solution of gelatin. It is made up of a complex mixture of ACTH, ACTH related peptides and other porcine pituitary derived peptides. It contains the porcine derived ACTH (1-39). Purified Cortrophin Gel is supplied sterile in 5 mL multiple-dose vials containing 80 USP units/mL.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Infantile spasms (also known as infantile epileptic spasms syndrome (IESS)):
Evidence of specific abnormal pattern detected by a video EEG with hypsarrhythmia

Response is defined as achieved and maintains complete cessation of spasms and elimination of hypsarrhythmia on a full sleep video EEG

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MS exacerbation:

Evidence of an attack with neurologic disturbances consistent with MS developing acutely or sub acutely with a duration of at least 24 hours, with or without recovery, and in the absence of fever or infection

MS exacerbation, relapse, flare, and attack are synonyms. The term "clinically isolated syndrome" (CIS) is also synonymous when used to denote the first clinical episode of MS; a CIS resembles a typical MS relapse but occurs in a patient not known to have MS.

Response is defined as **THREE** of the following:

- Mild/minimal to no functional neurologic (pyramidal, cerebellar, brainstem, sensory) disabilities
- Ambulatory without need for assistance
- Reduction in number of exacerbations or relapses of MS
- Prolonged time to exacerbation or relapses of MS
- Reduction in hospitalizations for MS

Resources:

Acthar Gel (repository corticotropin) product information, revised by Mallinckrodt ARD, LLC. 02-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 20, 2024.

Purified Cortrophin Gel (repository corticotropin) product information, revised by ANI Pharmaceuticals, Inc.10-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 20, 2024.

Takacs DS, Katyayan A. Infantile epileptic spasms syndrome: Management and prognosis. In: UpToDate, Nordli DR, Dashe JF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through October 2024. Topic last updated August 10, 2023. Accessed November 26, 2024.

Takacs DS, Katyayan A. Infantile epileptic spasms syndrome: Etiology and pathogenesis. In: UpToDate, Nordli DR, Dashe JF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through October 2024. Topic last updated June 14, 2024. Accessed November 26, 2024.

Olek MJ, Howard J. Treatment of acute exacerbations of multiple sclerosis in adults. In: UpToDate, Gonzalez-Scarano F, Dashe JF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through October 2024. Topic last updated April 30, 2024. Accessed November 26, 2024.

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