H.P. Acthar (corticotropin) Prior Approval Criteria
February 2016

OVERVIEW
Repository corticotropin injection (H.P. Acthar® Gel) (Questcor®, Union City, CA) is an injectable formulation of adrenocorticotropic hormone (ACTH) utilized for treatment of infantile spasms (IS) (West syndrome) and exacerbations of multiple sclerosis in adults.

Initial approval of Acthar in the US was in 1952. At that time, original approval only required that the medication was safe for human use. Current guidelines, reviews, or position papers from nationally recognized organizations discuss the role of Acthar in infantile spasms and MS. The Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines for glomerulonephritis note that ACTH has a limited role. Other reviews have been published regarding nephrotic syndrome but do not mention use of Acthar or note that experience with the agent is far too preliminary. The recommended authorization criteria address the use of Acthar in infantile spasms and MS exacerbations in adults. Regarding Acthar’s other uses, data and guidelines do not suggest that Acthar has a substantial role in therapy. Further data are needed before use in other areas can be recommended.

POLICY STATEMENT
Prior authorization is recommended for prescription benefit coverage of Acthar. The recommended authorization criteria address the use of Acthar in infantile spasms and MS exacerbations in adults. Because of the specialized skills required for evaluation and diagnosis of patients with these conditions, as well as monitoring required for adverse events (AEs) and efficacy, approval requires Acthar to be prescribed by, or in consultation with, a physician who specializes in the conditions being treated.

Recommended Authorization Criteria
Coverage of Acthar is recommended in those who meet the following criteria:

Food and Drug Administration (FDA)-Approved Indications

1. **Infantile spasms:** The Company considers repository corticotropin injection medically necessary and eligible for reimbursement providing that all of the following medical criteria are met:
   - Infantile spasms; and
   - Age <5 years of age; and
   - Diagnosis confirmed by electroencephalography; and
   - Dosage and administration are consistent with U.S. Food and Drug Administration approved label (i.e., 150 U/m² divided into twice daily intramuscular injections of 75 U/m²); and
   - Prescribed by or in consultation with a neurologist or epileptologist

2. **Multiple sclerosis:** The Company considers repository corticotropin injection medically necessary and eligible for reimbursement providing that all of the following medical criteria are met:
   - Acute exacerbation(s) of multiple sclerosis; and
   - Age >18 years; and
- Failure of, intolerance to or unable to receive high-dose corticosteroids administered intravenously (IV) (e.g., methylprednisolone 500 to 1,000 mg IV daily for three to five days). High-dose oral corticosteroids may be substituted; and

- Dosage and administration are consistent with U.S. Food and Drug Administration approved label (i.e., 80-120 units daily for a two to three week time period); and

- Prescribed by or in consultation with a neurologist or physician that specializes in the treatment of multiple sclerosis (MS)

**Frequency limitations:** The Company considers long-term use (>4 weeks) of repository corticotropin injection for treatment of multiple sclerosis **not medically necessary** and not eligible for reimbursement.

**Approval Duration**
All Approvals = 30 days (one month)

**Conditions Not Recommended for Approval**
Acthar has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

3. **Use in Patients with Multiple Sclerosis (MS) as “Pulse Therapy” on a Monthly Basis.** Preliminary data have investigated use of Acthar given as 80 units IM once a day for 3 days once a month. This is not an accepted use of Acthar and more data are needed.

4. **Treatment of Proteinuria in Diabetic Nephropathy.** Acthar is being investigated for this use. At this time, limited data are available and Acthar is not established for this use.

5. **Treatment of Nephrotic Syndrome.** The prescribing information for Acthar states that it may be used in an edematous state, such as 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. However, very limited data have studied the use of Acthar, in patients with diagnoses including idiopathic membranous nephropathy (iMN), membranoproliferative glomerulonephritis (MPGN), focal segmental glomerulosclerosis (FSGS), minimal change disease (MCD), immunoglobulin A (IgA) nephropathy, class V SLE glomerulonephritis, and monoclonal diffuse proliferative glomerulonephritis. Other data in nephrotic syndrome are available regarding use of a synthetic ACTH analog that is available in Europe (tetracosactide [Synacthen® Depot]). Limited data from a prospective, open-label trial were published involving 15 patients with resistant glomerular diseases who received Acthar 80 units SC twice weekly for 6 months; most patients had tried previous immunosuppressive therapy and/or steroids. Although some benefits were noted in selected patients (e.g., achievement of partial remission) the authors concluded that controlled studies should be performed against currently available therapies for resistant disease. Two reviews regarding the treatment of iMN notes that experience with ACTH in the US is far too preliminary to consider using this therapy for widespread use. In June 2012, KDIGO published clinical practice guidelines for glomerulonephritis. The guidelines state that the data involving ACTH is of low quality in iMN. The use of ACTH requires further study and data are insufficient to make specific recommendations. In 2013, the National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) organized a work group of experts to review the 2012 KDIGO guideline and comment on the recommendations in the
practice of nephrology in the US. Recommendations regarding Acthar are that ACTH (adrenocorticotrophic hormone) is not recommended as a steroid-like option in children as it has not been studied in this population with steroid-resistant nephrotic syndrome or in steroid-sensitive nephrotic syndrome. Among the treatment of resistant membranous nephropathy in adults, it is stated that the use of ACTH requires further study. The purified porcine ACTH agent approved in the US is a different formulation with alternative dosing compared with the synthetic agent that has been more adequately investigated in Europe. Only small studies have been performed with the US formulation. Data are very preliminary and do not yet support use of this treatment outside clinical research studies. It is not recommended to use ACTH for initial treatment of iMN at this time. AEs related to use of ACTH (myopathy, cataracts, hyperglycemia) are not insignificant. Issues that need to be studied with this medication include optimal dosing regimens, rate of relapse, and mechanisms of action. Additionally, guidelines from the American College of Rheumatology (ACR) for the screening, treatment and management of lupus nephritis, published in 2012, do not mention use of Acthar gel.

6. Dermatomyositis or Polymyositis. More recent data are limited to a five-patient retrospective case series detailing the effects of Acthar in patients with dermatomyositis and polymyositis. Controlled trials are needed before Acthar can be considered an established or recommended therapy. The idiopathic inflammatory myopathies are a group of rare, systemic connective tissue diseases that impact the muscles leading to proximal muscle weakness, muscle enzyme elevations and extramuscular manifestations (e.g., fever, rash), and include diagnoses such as adult polymyositis and dermatomyositis. The initial treatment approach in adult patients include high-dose corticosteroids (prednisone 0.5 to 1 mg/kg per day for 2 to 4 weeks) given with either methotrexate, azathioprine or mycophenolate mofetil. For patients with disease refractory to conventional therapy, agents used include IV methylprednisolone, intravenous immunoglobulin (IVIG), cyclophosphamide, Rituxan® (rituximab injection), and cyclosporine.

7. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES


**Other References Utilized**