Medication Policy Manual

**Policy No:** dru316

**Topic:** Acthar H.P.® Gel, repository corticotropin injection

**Date of Origin:** July 12, 2013

**Committee Approval Date:** June 12, 2015

**Next Review Date:** June 2016

**Effective Date:** July 1, 2015

**IMPORTANT REMINDER**

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

*Benefit determinations should be based in all cases on the applicable contract language.* To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

**Description**

Repository corticotropin (Acthar H.P.® gel) is a medication used to treat infantile spasms and a variety of inflammatory conditions. Repository corticotropin is a porcine-derived, extended release preparation of adrenocorticotropic hormone (ACTH). ACTH is a hormone in the body, which stimulates the adrenal cortex gland to secrete natural steroids (cortisol, corticosterone, and aldosterone). Please note that this policy does not apply to cosyntropin (generic Cortrosyn; also referred to as ACTH), which is used for cortisol-stimulation testing.
Policy/Criteria

I. Most contracts require prior authorization approval of repository corticotropin prior to coverage. Repository corticotropin may be considered medically necessary in patients with infantile spasms (West Syndrome) when prescribed by a pediatric neurologist or an epilepsy physician specialist. [ICD-9: 345.6]

II. Administration, Quantity Limitations, and Authorization Period
A. OmedaRx does not consider repository corticotropin to be a self-administered medication.
B. When prior authorization is approved, repository corticotropin may be authorized in quantities of six-5 ml vials per month.
C. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

III. Repository corticotropin is considered not medically necessary when used for the following conditions:
A. Dermatologic diseases including severe erythema multiforme, Stevens-Johnson syndrome, systemic dermatomyositis, and polymyositis.
B. Multiple sclerosis, acute exacerbation in adults.
C. Nephrotic syndrome, without uremia of the idiopathic type (idiopathic membranous nephropathy) or that due to lupus erythematosus.
D. Ophthalmic diseases including keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, anterior segment inflammation.
E. Rheumatic disorders including psoriatic arthritis, rheumatoid arthritis, including juvenile rheumatoid arthritis, ankylosing spondylitis.
F. Sarcoidosis (symptomatic)
G. Serum sickness
H. Systemic lupus erythematosus (SLE), exacerbation

IV. Repository corticotropin is considered investigational when used for all other conditions.
Position Statement

- Repository corticotropin was first approved for sale in the United States in 1952. It has been used in a number of different indications, though its use was largely supplanted by the commercial availability of corticosteroids (e.g. hydrocortisone, prednisone, methylprednisolone), all available as much lower-cost generics.

- Repository corticotropin is effective in the management of children with a rare seizure disorder known as infantile spasms.

- Although repository corticotropin is FDA approved for a variety of inflammatory conditions, these indications are grandfathered given trials establishing efficacy were not required at the time when repository corticotropin was originally approved. Still today, there is insufficient evidence to establish efficacy for these indications, or superiority to less costly alternatives (such as generic corticosteroids). Therefore the use of repository corticotropin for indications other than infantile spasms is considered not medically necessary. Specifically:
  
  o For multiple sclerosis, there is insufficient evidence to establish that repository corticotropin is superior to much less costly standard of care alternatives, such as standard “pulse” methylprednisolone therapy in the management of acute exacerbations.

  o For nephrotic syndrome (idiopathic or due to lupus), there is insufficient evidence to establish that repository corticotropin is superior to much less costly standard of care alternatives such as calcineurin inhibitors and cyclophosphamide, along with mycophenolate, and rituximab, all endorsed by clinical guidelines.

- Since repository corticotropin stimulates steroid production in the body, the warnings of repository corticotropin use is similar to those found with steroid supplementation, for example, impaired sugar tolerance and high blood sugars.

- Side effects or intolerance to corticosteroids are largely expected with the use of repository corticotropin given the medication stimulates steroid production in the body.

- In addition, the evidence for significant, previously unreported safety events with the use of repository corticotropin is evolving. Based on the available evidence, the safety of repository corticotropin relative to other therapies is unknown at this time.

Clinical Efficacy

Infantile Spasms

There is moderate certainty that repository corticotropin is safer and more effective than vigabatrin (Sabril®) in the management of patients with infantile spasms (aka West syndrome).

- A high-quality systematic review concluded that repository corticotropin (HP Acthar Gel) resulted in greater improvements in seizure frequency over 14 days compared with vigabatrin (Sabril) (76% vs 54%) [1,3].

- The systematic review also concluded that repository corticotropin (HP Acthar Gel) resulted in greater improvements in neurodevelopmental outcomes as measured by standardized behavioral scales. [1,3]
- Repository corticotropin is recognized by clinical practice guidelines as an option in the management of patients with infantile spasms, with repository corticotropin considered preferentially over vigabatrin. [1,3]

**Acute Exacerbations of Multiple Sclerosis**

- The use of repository corticotropin is considered not medically necessary when used for multiple sclerosis.
- Multiple sclerosis is an FDA-approved indication for repository corticotropin; however, corticosteroids, such as methylprednisolone and dexamethasone, are less costly alternatives.
- A head-to-head clinical trial compared a 14-day course of repository corticotropin with methylprednisolone 1 gm given intravenously daily for three days. At the end of twelve weeks, there was no statistically significant difference between the two regimens in the symptoms of multiple sclerosis as measured by the expanded disability symptom scale (EDSS or Kurtzke status scale). [4]
- A high-quality systematic review concluded that there was no evidence of improved symptoms or outcomes resulting from the use of repository corticotropin in the management of acute exacerbations of multiple sclerosis compared with standard “pulse” methylprednisolone therapy. [5]
- A more recent pilot trial (n=20) evaluated a 5-day course of repository corticotropin for management of acute MS exacerbations. However, because the comparison was two routes of administration of repository corticotropin (intramuscular versus subcutaneous), no conclusion can be made regarding the relative benefit of repository corticotropin versus other treatment options. [10]

**Nephrotic Syndrome**

- The use of repository corticotropin is considered not medically necessary when used for nephrotic syndrome, including membranous glomerulonephropathy.
- Nephrotic syndrome is an FDA-approved indication; however, there are multiple less costly alternatives supported by standard of care guidelines, including corticosteroids, calcineurin inhibitors, mycophenolate, and alkylating-based therapy (cyclophosphamide). [6]
- The evidence for the use of repository corticotropin for proteinuria/nephrotic syndrome is limited to case series and one pilot trial versus methylprednisolone + cytotoxic therapy, which found similar response to standard therapy vs. repository corticotropin. [7-9]

**Other indications**

- There is insufficient evidence for other indications (including, but not limited to, rheumatic disorders, systemic lupus erythematosus, dermatologic conditions, serum sickness, ophthalmic diseases, and pulmonary sarcoidosis) that treatment with repository corticotropin results in improved efficacy or safety when compared with other standard treatments. Therefore, use in all these indications is considered not medically necessary.
Safety
- There is a substantial track-record of marketing experience extending over 50 years with repository corticotropin. In pediatric patients, the length of market experience extends at least over five years. [1]
- Common adverse reactions for repository corticotropin 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. [1]
- Specific adverse reactions resulting from use of repository corticotropin in children less than 2 years of age are increased risk of infections, hypertension, irritability, Cushingoid symptoms, cardiac hypertrophy and weight gain. [1]
- Serious adverse events associated with repository corticotropin are also similar to those of corticosteroids and include increase susceptibility to infections, adrenal suppression after prolonged use, Cushing’s syndrome, gastrointestinal perforation and bleeding, and negative effects on growth and development. [1]

Dosing
- In the treatment of infantile spasms, the recommended dose is 150 units (U)/m² divided into twice daily intramuscular injections of 75 U/m². After 2 weeks of treatment, dosing should be gradually tapered and discontinued over a 2-week period.

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
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<tbody>
<tr>
<td>HCPCS</td>
<td>J0800</td>
<td>Injection, corticotropin, up to 40 units</td>
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<tr>
<td>CPT</td>
<td>345.6</td>
<td>Infantile spasms</td>
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</tbody>
</table>

Cross References
None

References
2. Sabril® [prescribing information]. Deerfield, IL: Lundbeck; February 2012


