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Mallinckrodt Statement on Treatment of Infantile Spasms During COVID-19

Mallinckrodt Pharmaceuticals has several options available to help patients with infantile spasms (IS) receive appropriate treatment and access to therapy, even in the midst of the COVID-19 pandemic.

Acthar® Gel (repository corticotropin injection) is recommended as a first-line treatment for IS.[1] High-dose, short duration therapy with Acthar Gel has been shown to eliminate both spasms and hypsarrhythmia across all etiologies of IS.[2,3]

Acthar Gel can be initiated in both a hospital and an out-patient setting, providing an important option for caregivers and healthcare providers who are concerned about patients entering a hospital setting during the pandemic. The most common reasons for inpatient initiation of Acthar Gel are electroencephalogram (EEG) test confirmation of the diagnosis and injection training, both of which can be conducted in an out-patient setting.[4]

A range of standard treatments, including Acthar Gel, can be administered in both hospital and outpatient settings, and physicians may consider this when making treatment decisions for patients with IS.

In addition, Mallinckrodt's Acthar Patient Support team has a long-established system of support for individual at-home (live or remote) injection training for parents/caregivers, as well as remote, virtual support from a Nurse Navigator and Case Manager. A dedicated Nurse Navigator provides patients and caregivers with one-on-one support throughout their treatment journey.

Mallinckrodt is committed to helping patients with IS access support for Acthar Gel in a safer way during this global health crisis. Please contact 1-800-778-7898 or visit our website for more information.

INDICATION

Acthar® Gel (repository corticotropin injection) is indicated as monotherapy for the treatment of infantile spasms in infants and children under 2 years of age

IMPORTANT SAFETY INFORMATION

Contraindications

- Acthar should never be administered intravenously
- Administration of live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of Acthar
- Acthar is contraindicated where congenital infections are suspected in infants
- Acthar is contraindicated in patients with 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

Warnings and Precautions

- The adverse effects of Acthar are related primarily to its steroidogenic effects
- Acthar may increase susceptibility to new infection or reactivation of latent infections
- Suppression of the hypothalamic-pituitary-adrenal (HPA) axis may occur following prolonged therapy with the potential for adrenal insufficiency after withdrawal of the medication. Adrenal insufficiency may be minimized by tapering of the dose when discontinuing treatment. During recovery of the adrenal gland patients should be protected from the stress (e.g. trauma or surgery) by the use of corticosteroids. Monitor patients for effects of HPA suppression after stopping treatment
- Cushing's syndrome may occur during therapy but generally resolves after therapy is stopped. Monitor patients for signs and symptoms
- Acthar can cause elevation of blood pressure, salt and water retention, and hypokalemia. Blood pressure, sodium, and potassium levels may need to be monitored
- Acthar often acts by masking symptoms of other diseases/disorders. Monitor patients carefully during and for a period following discontinuation of therapy
- Acthar can cause GI bleeding and gastric ulcer. There is also an increased risk for perforation in patients with certain gastrointestinal disorders. Monitor for signs of bleeding
- Acthar may be associated with central nervous system effects ranging from euphoria, insomnia, irritability, mood swings, personality changes, and severe depression to psychosis. Existing conditions may be aggravated
- Patients with comorbid disease may have that disease worsened. Caution should be used when prescribing Acthar in patients with diabetes and myasthenia gravis
- Prolonged use of Acthar may produce cataracts, glaucoma, and secondary ocular infections. Monitor for signs and symptoms
- Acthar is immunogenic and prolonged administration of Acthar may increase the risk of hypersensitivity reactions. Neutralizing antibodies with chronic administration may lead to loss of endogenous ACTH activity
- There is an enhanced effect in patients with hypothyroidism and in those with cirrhosis of the liver
- Long-term use may have negative effects on growth and physical development in children. Monitor pediatric patients
- Decrease in bone density may occur. Bone density should be monitored for patients on long-term therapy
- Pregnancy Class C: Acthar has been shown to have an embryocidal effect and should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus

Adverse Reactions

- Common adverse reactions for Acthar 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
- Specific adverse reactions reported in IS clinical trials in infants and children under 2 years of age included: infection, hypertension, irritability, Cushingoid symptoms,

constipation, diarrhea, vomiting, pyrexia, weight gain, increased appetite, decreased appetite, nasal congestion, acne, rash, and cardiac hypertrophy. Convulsions were also reported, but these may actually be occurring because some IS patients progress to other forms of seizures and IS sometimes masks other seizures, which become visible once the clinical spasms from IS resolve

Other adverse events reported are included in the full Prescribing Information.

Please see full Prescribing Information for additional Important Safety Information.

References

[1] Mackay, M.T., et al. Practice Parameters: Medical Treatment of Infantile Spasms. Report of the American Academy of Neurology and the Child Neurology Society. *Neurology*. 2004. 62.
[2] Baram TZ, Mitchell WG, Tournay A, Snead OC III, Hanson RA, Horton EJ. High-dose corticotropin (ACTH) versus prednisone for infantile spasms: a prospective, randomized, blinded study. *Pediatrics.* 1996;97(3):375-379.
[3] Acthar® Gel (repository corticotropin injection) [prescribing information]. Mallinckrodt ARD LLC.
[4] Joshi C., Berg A. T., Wirrell E. Do Patients Require Inpatient Admission to Receive Adrenocorticotropic Hormone (ACTH)? A Survey of US-Based Prescribers*. Journal of Child Neurology*. 2015;31(2):164-169.