HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use H.P. Acthar® Gel safely and effectively. See full prescribing information for H.P. Acthar Gel.

H.P. Acthar Gel (repository corticotropin injection) INJECTION, GEL FOR INTRAMUSCULAR | SUBCUTANEOUS use
Initial U.S. Approval: 1952

INDICATIONS AND USAGE
• H.P. Acthar Gel is an adrenocorticotropic hormone (ACTH) analogue indicated as monotherapy for the treatment of infantile spasms in infants and children under 2 years of age. (1.1)
• H.P. Acthar Gel is indicated for the treatment of exacerbations of multiple sclerosis in adults. (1.2)
• H.P. Acthar Gel may be used for the following disorders and diseases: rheumatic; collagen; dermatologic; allergic states; ophthalmic; respiratory; and edematous state. (1.3 to 1.9)

DOSEAGE AND ADMINISTRATION
In the treatment of infantile spasms, the recommended dose is 150 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. (1.1)
In the treatment of acute exacerbations of multiple sclerosis, daily intramuscular or subcutaneous doses of 80-120 units for 2-3 weeks may be administered. It may be necessary to taper the dose. (2.1)
In the treatment of other disorders and diseases, dosing will need to be individualized depending on the disease under treatment and the medical condition of the patient. It may be necessary to taper the dose. (2.2)

DOSE FORMS AND STRENGTHS
• 5 mL multi-dose vial containing 80 USP units per mL (3)

CONTRAINDICATIONS
• H.P. Acthar Gel should never be given intravenously.
• H.P. Acthar Gel 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, or sensitivity to proteins of porcine origin.
• Administration of live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of H.P. Acthar Gel.
• H.P. Acthar Gel is contraindicated in children under 2 years of age with suspected congenital infections. (4)
• Treatment of conditions listed within the INDICATIONS AND USAGE section is contraindicated when they are accompanied by primary adrenocortical insufficiency or adrenocortical hyperfunction. (4)

WARNINGS AND PRECAUTIONS
Infections: Increased susceptibility to new infection and increased risk of exacerbation, dissemination or reactivation of latent infections. Signs and symptoms of infection may be masked. (5.1)
Adrenal Insufficiency after Prolonged Therapy: Monitor for effects of hypothalamic-pituitary-axis suppression after stopping treatment. (5.2)
Cushing’s Syndrome: May occur after prolonged therapy. Monitor for signs and symptoms. (5.2)

ADVERSE REACTIONS
Common adverse reactions for H.P. Acthar Gel 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. (6)
Special adverse reactions resulting from drug use in children under 2 years of age are increased risk of infections, hypertension, irritability, Cushingoid symptoms, cardiac hypertrophy and weight gain. (6.1.1)

USE IN SPECIFIC POPULATIONS
Pediatric Use: Prolonged use of H.P. Acthar Gel in children may inhibit skeletal growth. If use is necessary, it should be given intermittently with careful observation. (7.12 and 8.4)

See 17 for Patient Counseling Information and FDA-approved Medication Guide

Revised: July 2017

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Infantile spasms:
H.P. Acthar Gel (repository corticotropin injection) is indicated as monotherapy for the treatment of infantile spasms in infants and children under 2 years of age.

1.2 Multiple Sclerosis:
H.P. Acthar Gel (repository corticotropin injection) is indicated for the treatment of acute exacerbations of multiple sclerosis in adults. Controlled clinical trials have shown H.P. Acthar Gel to be effective in speeding the resolution of acute exacerbations of multiple sclerosis. However, there is no evidence that it affects the ultimate outcome or natural history of the disease.

1.3 Rheumatic Disorders:
As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in: Psoriatic arthritis, Rheumatoid arthritis, juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy), Ankylosing spondylitis.

1.4 Collagen Diseases:
During an exacerbation or as maintenance therapy in selected cases of: systemic lupus erythematosus, systemic dermatomyositis (polymyositis).

1.5 Dermatologic Diseases:
Severe erythema multiforme, Stevens-Johnson syndrome.

1.6 Allergic States:
Serum sickness.

1.7 Ophthalmic Diseases:
Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis; anterior segment inflammation.

1.8 Respiratory Diseases:
Symptomatic sarcoidosis.

1.9 Edematous State:
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.

2 DOSAGE AND ADMINISTRATION

2.1 Specific Recommended Dosage Regimen for Infantile Spasms in Infants and Children Under 2 Years of Age
In the treatment of infantile spams, H.P. Acthar Gel must be administered intramuscularly. The recommended regimen is a daily dose of 150 U/m2 divided into twice daily intramuscular injections of 75 U/m2 administered over a 2-week period. Dosing with H.P. Acthar Gel should then be gradually tapered over a 2-week period to avoid adrenal insufficiency. The following is one suggested tapering schedule: 30 U/m2 in the morning for 3 days; 15 U/m2 in the morning for 3 days; 10 U/m2 in the morning for 3 days; and 5 U/m2 every other morning for 6-days.

H.P. Acthar Gel is typically dosed based on body surface area (BSA). For calculation of body surface area, use the following formula:

\[ BSA(m^2) = \sqrt{\frac{\text{weight (kg)} \times \text{height (cm)}}{3600}} \]

2.2 Recommended Dosage Regimen for the Treatment of Acute Exacerbations in Adults with Multiple Sclerosis
The recommended dose is daily intramuscular or subcutaneous doses of 80-120 units for 2-3 weeks for acute exacerbations.

Dosage should be individualized according to the medical condition of each patient. Frequency and dose of the drug should be determined by considering the severity of the disease and the initial response of the patient.

Although drug dependence does not occur, sudden withdrawal of H.P. Acthar Gel after prolonged use may lead to adrenal insufficiency or recurrent symptoms which make it difficult to stop the treatment. It may be necessary to taper the dose and increase the injection interval to gradually discontinue the medication.

2.3 Recommended Dosage Regimen for Other Indications for Adults and Children Over 2 Years of Age
Dosage should be individualized according to the disease under treatment and the general medical condition of each patient. Frequency and dose of the drug should be determined by considering severity of the disease and the initial response of the patient.

The usual dose of H.P. Acthar Gel is 40-80 units given intramuscularly or subcutaneously every 24-72 hours.

Although drug dependence does not occur, sudden withdrawal of H.P. Acthar Gel after prolonged use may lead to adrenal insufficiency or recurrent symptoms which make it difficult to stop the treatment. It may be necessary to taper the dose and increase the injection interval to gradually discontinue the medication.

2.4 Preparation
H.P. Acthar Gel should be warmed to room temperature before using.

Caution should be taken not to over-pressurize the vial prior to withdrawing the product.

3 DOSAGE FORMS AND STRENGTHS
5 mL multidose vial containing 80 USP Units per mL.

4 CONTRAINDICATIONS
H.P. Acthar Gel is contraindicated for intravenous administration.

H.P. Acthar Gel is contraindicated where congenital infections are suspected in infants.

Administration of live or live attenuated vaccines is contraindicated in patients receiving immunsuppressive doses of H.P. Acthar Gel.

H.P. Acthar Gel 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.

5 WARNINGS AND PRECAUTIONS
The adverse effects of H.P. Acthar Gel are related primarily to its steroidogenic effects. Not all of the adverse events described below have been seen after treatment with H.P. Acthar Gel, but might be expected to occur. [see Adverse Reactions (6.3)]

5.1 Infections
H.P. Acthar Gel may increase the risks related to infections with any pathogen, including viral, bacterial, fungal, protozoan or helminthic infections. Patients with latent tuberculosis or tuberculosis reactivity should be observed closely, and if therapy is prolonged, chemoprophylaxis should be instituted.

5.2 Cushion's Syndrome and Adrenal Insufficiency Upon Withdrawal
Treatment with H.P. Acthar Gel can cause hypothalamic-pituitary-axes (HPA) suppression and Cushion's syndrome. These conditions should be monitored especially with chronic use.

Suppression of the HPA may occur following prolonged therapy with the potential for adrenal insufficiency after withdrawal of the medication. Patients should be monitored for signs of insufficiency such as weakness, hyperpigmentation, weight loss, hypotension and abdominal pain.

The symptoms of adrenal insufficiency in infants treated for infantile spasms can be difficult to identify. The symptoms are non-specific and may include anorexia, fatigue, lassitude, weakness, excessive weight loss, hypotension and abdominal pain. It is critical that parents and caregivers be made aware of the possible of adrenal insufficiency when discontinuing H.P. Acthar Gel and should be instructed to observe for, and be able to recognize, these symptoms. [see Patient Counseling Information (17)]

The recovery of the adrenal gland may take from days to months so patients should be protected from the stress (e.g. trauma or surgery) by the use of corticosteroids during the period of stress.

The adrenal insufficiency may be minimized in adults and infants by tapering of the dose when discontinuing treatment.

Signs or symptoms of Cushion's syndrome may occur during therapy but generally resolve after therapy is stopped. Patients should be monitored for these signs and symptoms such as deposition of adipose tissue in characteristics sites (e.g., moon face, truncal obesity), cutaneous striae, easy bruising, decreased bone mineralization, weight gain, muscle weakness, hyperglycemia, and hypertension.

5.3 Elevated Blood Pressure, Salt and Water Retention and Hypokalemia
H.P. Acthar Gel can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium and calcium. Dietary salt restriction and potassium supplementation may be necessary. Caution should be used in the treatment of patients with hypertension, congestive heart failure, or renal insufficiency.

5.4 Vaccination
Administration of live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of H.P. Acthar Gel. Killed or inactivated vaccines may be administered; however, the response to such vaccines can not be predicted. Other immunization procedures should be undertaken with caution in patients who are receiving H.P. Acthar Gel, especially when high doses are administered, because of the possible hazards of neurological complications and lack of antibody response.

5.5 Masking Symptoms of Other Diseases
H.P. Acthar Gel often acts by masking symptoms of other diseases/disorders without altering the course of the other disease/disorder. Patients should be monitored carefully during and for a period following discontinuation of therapy for signs of infection, abnormal cardiac function, hyperglycemia, change in body weight and fecal blood loss.

5.6 Gastrointestinal Perforation and Bleeding
H.P. Acthar Gel can cause GI bleeding and gastric ulcer. There is also an increased risk for perforation in patients with certain gastrointestinal disorders. Signs of gastrointestinal perforation such as peritoneal irritation, may be masked by the therapy. Use caution where there is the possibility of impending perforation, abscess or other pyogenic infections, diverticulitis, fresh intestinal anastomoses, and active or latent peptic ulcer.

5.7 Behavioral and Mood Disturbances
Use of H.P. Acthar Gel may be associated with central nervous system effects ranging from euphoria, insomnia, irritability (especially in infants), mood swings, personality changes, and severe depression, to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated.

5.8 Comorbid Diseases
Patients with a comorbid disease may have that disease worsened. Caution should be used when prescribing H.P. Acthar Gel in patients with diabetes and myasthenia gravis.

5.9 Ophthalmic Effects
Prolonged use of H.P. Acthar Gel may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves and may enhance the establishment of secondary ocular infections due to fungi and viruses.
5.10 Immunogenicity Potential
H.P. Acthar Gel is immunogenic. Limited available data suggest that a patient may develop antibodies to H.P. Acthar Gel after chronic administration and loss of endogenous ACTH and H.P. Acthar Gel activity. Prolonged administration of H.P. Acthar Gel may increase the risk of hypersensitivity reactions. Sensitivity to porcine protein should be considered before starting therapy and during the course of treatment should symptoms arise.

5.11 Use in Patients with Hypothyroidism or Liver Cirrhosis
There is an enhanced effect in patients with hypothyroidism and in those with cirrhosis of the liver.

5.12 Negative Effects on Growth and Physical Development
Long-term use of H.P. Acthar Gel may have negative effects on growth and physical development in children. Changes in appetite are seen with H.P. Acthar Gel therapy, with the effects becoming more frequent as the dose or treatment period increases. These effects are reversible once H.P. Acthar Gel therapy is stopped. Growth and physical development of pediatric patients on prolonged therapy should be carefully monitored.

5.13 Decrease in Bone Density
Decrease in bone formation and an increase in bone resorption both through an effect on calcium regulation (i.e. decreasing absorption and increasing excretion) and inhibition of osteoblast function may occur. These, together with a decrease in the protein matrix of the bone (secondary to an increase in protein catabolism) and reduced sex hormone production, may lead to inhibition of bone growth in children and adolescents and to the development of osteoporosis at any age. Special consideration should be given to patients at increased risk of osteoporosis (i.e., postmenopausal women) before initiating therapy, and bone density should be monitored in patients on long-term therapy.

5.14 Use in Pregnancy
H.P. Acthar Gel has been shown to have an embryocidal effect. Apprise women of potential harm to the fetus. [See Use in Specific Populations (8.11)]

6 ADVERSE REACTIONS
Please refer to Adverse Reactions in Infants and Children Under 2 Years of Age (Section 6.1.1) for consideration when treating patients with Infantile Spasms. The adverse reactions presented in Section 6.2 are primarily provided for consideration in use in adults and in children over 2 years of age, but these adverse reactions should also be considered when treating infants and children under 2 years of age.

H.P. Acthar Gel causes the release of endogenous cortisol from the adrenal gland. Therefore all the adverse effects known to occur with elevated cortisol may occur with H.P. Acthar Gel administration as well. Common adverse reactions include fluid retention, alteration in glucose tolerance, elevation in blood pressure, behavioral and mood changes, increased appetite and weight gain.

6.1 Clinical Studies Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug, and may not reflect the rates observed in practice.

6.1.1 Adverse Reactions in Infants and Children Under 2 Years of Age
While the types of adverse reactions seen in infants and children under 2 years of age treated for infantile spasms are similar to those seen in older patients, their frequency and severity may be different due to the very young age of the infant, the underlying disorder, the duration of therapy and the dosage regimen. Below is a summary of adverse reactions specifically tabulated from source data derived from retrospective chart reviews and treated infants and children under 2 years of age.

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Recommended 75 U/m² bid n=122, (%)</th>
<th>150 U/m² gd n=37 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous system disorders</td>
<td>Convulsion1 12 3</td>
<td></td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>Nasal Congestion 1 5</td>
<td></td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Acne 0 14</td>
<td></td>
</tr>
<tr>
<td>Vascular disorders</td>
<td>Rash 0 8</td>
<td></td>
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<tr>
<td>Hypertension 11 19</td>
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</tbody>
</table>

*Specific infections that occurred at ≥2% were candidiasis, otitis media, pneumonia and upper respiratory tract infections. In the treatment of Infantile Spasms, other types of seizures/convulsions may occur because some patients with infantile spasms progress to other forms of seizures (for example, Lennox-Gastaut Syndrome). Additionally the spasms sometimes mask other seizures and once the spasms resolve after treatment, the other seizures may become visible.

These adverse reactions may also be seen in adults and children over 2 years of age when treated for other purposes and with different doses and regimens.

6.2 Postmarketing Experience
The following adverse reactions associated with the use of H.P. Acthar Gel have been identified from postmarketing experience with H.P. Acthar Gel. Only adverse events that are not listed above or as adverse events reported from retrospective chart reviews and non-sponsor conducted clinical trials and those not discussed elsewhere in labeling, are listed in this section. Because the adverse reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency or establish a causal relationship to use with H.P. Acthar Gel. Events are categorized by system organ class. Unless otherwise noted these adverse events have been reported in adults, children and children.

6.2.1 Allergic Reactions
Allergic responses have presented as dizziness, nausea and shock (adults only).

6.2.2 Cardiovascular
Necrotizing angitis (adults only) and congestive heart failure.

6.2.3 Dermatologic
Skin thinning (adults only), facial erythema and increased sweating (adults only).

6.2.4 Endocrine
Decrease carbohydrate tolerance (infants only) and hirsutism.

6.2.5 Gastrointestinal
Pancreatitis (adults only), abdominal distention and ulcerative esophagitis.

6.2.6 General disorders and administration site conditions
Injection site reactions (adults only).

6.2.7 Metabolic
Hypokalemic alkalosis (infants only).

6.2.8 Musculoskeletal
Muscle weakness and vertebral compression fractures (infants only).

6.2.9 Neurological
Headache (adults only), vertigo (adults only), subdural hematoma, intracranial hemorrhage (adults only), and reversible brain shrinkage (usually secondary to hypertension)(infants only).

6.3 Possible Additional Steroidogenic Effects
Based on steroidogenic effects of H.P. Acthar Gel certain adverse events may be expected due to the pharmacological effects of corticosteroids. The adverse events that may occur but have not been reported for H.P. Acthar Gel are:

6.3.1 Dermatologic
Impaired wound healing, abscess, petechiae and ecchymoses, and suppression of skin test reactions.

6.3.2 Endocrine
Menstrual irregularities.

6.3.3 Metabolic
Negative nitrogen balance due to protein catabolism.

6.3.4 Musculoskeletal
Loss of muscle mass and aseptic necrosis of femoral and humeral heads.

6.3.5 Neurological
Increased intracranial pressure with papilledema, (pseudo-tumor cerebri) usually after treatment, and subdural effusion.

6.3.6 Ophthalmic
Exophthalmos.

7 DRUG INTERACTIONS
Formal drug-drug interaction studies have not been performed.

H.P. Acthar Gel may accentuate the electrolyte loss associated with diuretic therapy.
Increased intracranial pressure with papilledema, (pseudo-tumor cerebri) usually after Based on steroidogenic effects of H.P. Acthar Gel certain adverse events may be expected the infusion. corticosteroid feedback mechanism. Elevated plasma cortisol suppresses ACTH release. H.P. Acthar Gel and endogenous ACTH stimulate the adrenal cortex to secrete corticosterone, aldosterone, and a number of weakly androgenic substances. 12 CLINICAL PHARMACOLOGY

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Pregnancy Class C. H.P. Acthar Gel has been shown to have an embryocidal effect. There are no adequate and well-controlled studies in pregnant women. H.P. Acthar Gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers
H.P. Acthar Gel is indicated as monotherapy for the treatment of infantile spasms in infants and children less than 2 years of age. Both serious and other adverse reactions in this population are discussed in Warnings and Adverse Reactions in Infants and Children Under 2 Years of Age [see Sections 5 and 6.1]. The efficacy of H.P. Acthar Gel for the treatment of infantile spasms in infants and children less than 2 years of age was evaluated in a randomized, single blinded (video EEG interpreter blinded) clinical trial and an additional active control supportive trial [see Clinical Studies (14)]. A responding patient was defined as having both complete cessation of spasms and elimination of hypersomnolence.

Safety in the pediatric population for infantile spasms was evaluated by retrospective chart reviews and data from non-sponsor conducted clinical trials [see Adverse Reactions (8.1.1)]. While the types of adverse reactions seen in infants and children under 2 years of age treated for infantile spasms are similar to those seen in older patients, their frequency and severity may be different due to the very young age of the infant, the underlying disorder, the duration of therapy and the dosage regimen. Effects on growth are of particular concern [see Warnings and Precautions (5.12)]. Serious adverse reactions observed in adults may also occur in children [see Warnings and Precautions (5)].

10 OVERDOSAGE
While chronic exposure to H.P. Acthar Gel at high doses can be associated with a variety of potential serious adverse effects, it is not expected that a single high dose, or even several large doses, has the potential for serious adverse effects compared to a standard dose. There have been no reports of death or acute overdose symptoms from H.P. Acthar Gel in children or in the published literature.

The intramuscular route of administration makes it unlikely that an inadvertent acute overdose will occur. The typical daily dose of H.P. Acthar Gel to treat an infant that has a BSA of 0.4 m² would be 60 U/day. Using the 1-c.c. syringe supplied with H.P. Acthar Gel, the maximum amount that can be injected is 80 U/injection, which is a well-tolerated single dose. 11 DESCRIPTION

H.P. Acthar Gel is a highly purified sterile preparation of the adrenocorticotropic hormone in 16% gelatin to provide a prolonged release after intramuscular or subcutaneous injection. Also contains 0.5% phenol, not more than 0.1% cocaine (added), sodium hydroxide and/or acetic acid to adjust pH and water for injection.

ACTH is a 39 amino acid peptide with the following chemical formula:

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<tr>
<th>H</th>
<th>Ser</th>
<th>Tyr</th>
<th>Ser</th>
<th>Met</th>
<th>Glu</th>
<th>His</th>
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</table>

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
The mechanism of action of H.P. Acthar Gel in the treatment of infantile spasms is unknown.

H.P. Acthar Gel and endogenous ACTH stimulate the adrenal cortex to secrete cortisol, corticosterone, aldosterone, and a number of weakly androgenic substances. Prolonged administration of large doses of H.P. Acthar Gel induces hyperplasia and hypertrophy of the adrenal cortex and continuous high output of cortisol, corticosterone and weakly androgenic substances. The release of endogenous ACTH is under the influence of the nervous system via the regulatory hormone released from the hypothalamus and by a negative corticosteroid feedback mechanism. Elevated plasma cortisol suppresses ACTH release. H.P. Acthar Gel is also reported to bind to melanocortin receptors. The trophic effects of endogenous ACTH and H.P. Acthar Gel on the adrenal cortex are not well understood beyond the fact that they appear to be mediated by cyclic AMP. ACTH rapidly disappears from the circulation following its intravenous administration; in people, the plasma half-life is about 15 minutes. The pharmacokinetics of H.P. Acthar Gel have not been adequately characterized. The maximal effects of a trophic hormone on a target organ are achieved when optimal amounts of hormone are acting continuously. Thus, a fixed dose of H.P. Acthar Gel will demonstrate a linear increase in adrenocortical secretion with increasing duration for the infusion.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Adverse have not been done in animals. Human use has not been associated with an increase in malignant disease. [see Warnings and Precautions (5.14) and Use in Specific Populations (8.1)].

14 CLINICAL STUDIES
The effectiveness of H.P. Acthar Gel as a treatment for infantile spasms was demonstrated in a single blinded (video EEG interpreter blinded) clinical trial in which patients were randomized to receive either a 2 week course of treatment with H.P. Acthar Gel (75 U/m² intramuscular twice daily) or prednisone (1 mg/kg by mouth twice daily). The primary outcome was a comparison of the number of patients in each group who were treatment responders, defined as a patient having complete suppression of both clinical and hypersomnolence on a full sleep cycle video EEG performed 2 weeks following treatment initiation, rated by an investigator blinded to treatment. Thirteen of 15 patients (86.7%) responded to H.P. Acthar Gel as compared to 4 of 14 patients (28.6%) given prednisone (p<0.002). The 2-week treatment was followed by a 2-week period of taper. Nonresponders (defined as in the previously described study) in the low-dose group received a dose escalation at 2 weeks to 30 U once daily. Nominal statistical superiority of the high dose treatment, as compared to the low dose treatment, was observed for cessation of spasms but not for the resolution of hypersomnolence.

15 HOW SUPPLIED / STORAGE AND HANDLING
H.P. Acthar Gel (repository corticotropin injection) is supplied as 5 mL multi-dose vial (63004-9710-1) containing 80 USP Units/ml. H.P. Acthar Gel (repository corticotropin injection) should be warmed to room temperature before using. Do not overpressurize the vial prior to withdrawing the product.

Store H.P. Acthar Gel (repository corticotropin injection) under refrigeration between 15°C (59°F) and 30°C (86°F). Product is stable for the period indicated on the label when stored under the conditions described.

17 PATIENT COUNSELING INFORMATION
Caregivers of patients with infantile spasms should be informed of the availability of a Medication Guide, and they should be instructed to read the Medication Guide prior to administering H.P. Acthar Gel. Patients should be instructed to take H.P. Acthar Gel as prescribed. They should not stop treatment suddenly unless instructed by their physician to do so.

Patients, their caregivers and families should be advised as to the importance of the need for careful monitoring while on and during titration from H.P. Acthar Gel treatment and the importance of not missing scheduled doctor’s appointments.

Patients, their caregivers and families should be advised that if the patient develops an infection or fever they should contact their physician. They should be educated that a fever may not necessarily be present during infection. The patient should also try to limit contact with other people with infection to minimize the risk of infection. If a fever is present, H.P. Acthar Gel should be continued [see Warnings and Precautions (5.1) and Adverse Reactions (6.1)].

Patients, their caregivers and families should be advised that if the patient experiences an increase in blood pressure they should contact their physician. [see Warnings and Precautions (5.3) and Adverse Reactions (6.1)].

Patients, their caregivers and families should be advised that if the patient or the caregiver notices blood or a change in color of the patient’s stool they should contact their physician. [see Warnings and Precautions (5.6)].

Caregivers and families of infants and children treated with H.P. Acthar Gel should be informed that the patient may show signs of irritability and sleep disturbances. These effects are reversible once H.P. Acthar Gel therapy is stopped. [see Warnings and Precautions (5.7) and Adverse Reactions (6.1)].

Patients, their caregivers and families should be advised that changes in appetite, most often leading to weight gain, are seen with H.P. Acthar Gel therapy, becoming more frequent as the dose or treatment period increases. These effects are reversible once H.P. Acthar Gel therapy is stopped. [see Warnings and Precautions (5.12) and Adverse Reactions (6.1)].

Patients, their caregivers and families should be advised that the patient may be monitored for signs of adrenal insufficiency such as weakness, fatigue, lethargy, anorexia, weight loss, hypotension, abdominal pain or hyperpigmentation (adults only) after treatment has been stopped. Since the recovery of the adrenal gland may take several months to years, patients may need to be protected from the stress of trauma or surgery by the use of corticosteroids during the period of stress. [see Warnings and Precautions (5.2)].

Patients should be advised not to be vaccinated with live or live attenuated vaccines during treatment with H.P. Acthar Gel. Additionally, other immunization procedures in patients or in family members who will be in contact with the patient should be undertaken with caution while the patient is taking H.P. Acthar Gel. [see Warnings and Precautions (5.4)].

Patients, their caregivers and families should be advised that prolonged use of H.P. Acthar Gel in children may result in the child’s growth and associated adverse reactions, may inhibit skeletal growth, and may cause osteoporosis and decreased bone density. If prolonged use is necessary, H.P. Acthar Gel should be given intermittently along with careful observation. [see Warnings and Precautions (5.2), (5.12), and (5.13) and Adverse Reactions (6.1)].
Patients, their caregivers and families should be informed that H.P. Acthar Gel may mask symptoms of other diseases/disorders without altering the course of the other disease/disorder. The patient will need to be monitored carefully during and for a period following discontinuation of therapy for signs of infection, abnormal cardiac function, hypertension, hyperglycemia, change in body weight, and fecal blood loss. (see Warnings and Precautions (5.5))

In the treatment of Infantile Spasms, other types of seizures may occur because some patients with infantile spasms progress to other forms of seizures (for example, Lennox-Gastaut Syndrome). Additionally the spasms sometimes mask other seizures and once the spasms resolve after treatment with H.P. Acthar Gel, the other seizures may become visible. Parents and caregivers should inform their physician of any new onset of seizures so that appropriate management can then be instituted. (see Adverse Reactions (6.1.1))

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