**Materials Organization Mat**

*Organize the injection materials before starting.* You may find it useful to lay the materials on this mat. That way, it’s easier to follow along with the Step-by-Step Injection Guide from your Starter Kit.

An injection training video is available online at [www.ActharInjectionTraining.com](http://www.ActharInjectionTraining.com).

If you have any additional questions, please contact your doctor or healthcare team.

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Please see Indication and Important Safety Information on back, as well as accompanying full Prescribing Information and Medication Guide.
WHAT IS ACTHAR GEL?

Acthar® Gel (repository corticotropin injection) is a prescription medicine that is used to treat infantile spasms in infants and children under 2 years of age. Acthar Gel is given as an injection into the muscle. Do not inject it under the skin, into a vein, or give it to your child by mouth.

IMPORTANT SAFETY INFORMATION

DO NOT take Acthar until you have talked to your doctor if you have any of the following conditions:

- A skin condition called scleroderma
- Bone density loss or osteoporosis
- Any infections, including fungal, bacterial, or viral
- Eye infections, such as ocular herpes simplex
- Had recent surgery
- Stomach ulcers or a history of stomach ulcers
- Heart failure
- Uncontrolled high blood pressure
- Allergies to pig-derived proteins
- Have been given or are about to receive a live or live attenuated vaccine
- Suspected congenital infections (in children under 2 years of age)
- If you have been told that you have Cushing's syndrome or Addison's disease

Tell your doctor about any other health problems that you have. Give your doctor a complete list of medicines you are taking. Include all nonprescription medicines, vitamins, and herbal supplements that you are taking.

What is the most important information I should know about Acthar?

- Never inject Acthar directly into a vein, under the skin, or give it to your child by mouth
- Always inject Acthar into the muscle
- Follow your doctor's instructions for injecting Acthar
- Never stop treatment suddenly unless your doctor tells you to do so
- Try not to miss any scheduled doctor's appointments. It is important for the doctor to monitor you while taking Acthar

Acthar and corticosteroids have similar side effects.

- You may be more likely to get new infections. Also, old infections may become active. Tell your doctor if you see any signs of an infection. Contact your doctor at the first sign of an infection or fever. Signs of infection are fever, cough, vomiting, or diarrhea. Other signs may be flu or any open cuts or sores
- When taking Acthar long term, your adrenal gland may produce too much of a hormone called cortisol. This can result in symptoms of Cushing's syndrome. This may cause increased upper body fat, a rounded "moon" face, bruising easily, or muscle weakness
- Sometimes when you stop taking Acthar long term, your body may not produce enough natural cortisol. This is called "adrenal insufficiency." Your doctor may prescribe a steroid medicine to protect you until the adrenal gland recovers
- You might develop high blood pressure, or retain too much fluid. As a result of this, your doctor may recommend some changes to your diet, such as eating less salt and taking certain supplements
- Vaccines may not work well when you are on Acthar. Talk to your doctor about which vaccines are safe to use when you are taking Acthar
- Acthar may hide symptoms of other diseases. This can make it more difficult for your doctor to make a diagnosis if something else is going on
- Stomach or intestinal problems. Acthar may increase the risk of bleeding stomach ulcers. Tell your doctor if you have stomach pains, bloody vomit, bloody or black stools, excessive tiredness, increased thirst, difficulty breathing, or increased heart rate
- Taking Acthar can make you feel irritable or depressed. You may also have mood swings or trouble sleeping
- If you have other conditions, such as diabetes or muscle weakness, you may find they get worse
- You might develop certain eye conditions, such as cataracts, glaucoma, or optic nerve damage
- Your body may develop allergies to Acthar. Signs of allergic reaction are:
  - Skin rash and itching
  - Swelling of the face, tongue, lips, or throat
  - Trouble breathing
- Long-term Acthar use can affect growth and physical development in children. This can be reversed when Acthar is no longer needed
- Acthar may cause osteoporosis (weak bones)
- Acthar should not be given to adults who are pregnant or plan to become pregnant

What are the most common side effects of Acthar?

The most common side effects of Acthar are similar to those of steroids. They include:

- Fluid retention
- High blood sugar
- High blood pressure
- Behavior and mood changes
- Changes in appetite and weight

Specific side effects in children under 2 years of age include:

- Increased risk of infections
- High blood pressure
- Irritability
- Symptoms of Cushing's syndrome
- Thickening of the heart muscle (cardiac hypertrophy)
- Weight gain

The above side effects may also be seen in adults and children over 2 years of age.

These are not all of the possible side effects of Acthar.

Tell your doctor about any side effect that bothers you, or that does not go away. Call your doctor or pharmacist for medical advice about side effects. You may report side effects to the FDA. Call 1-800-FDA-1088 or visit www.fda.gov/medwatch. You may also report side effects by calling 1-800-844-2830.

Please see accompanying full Prescribing Information.

For parents and caregivers of IS patients, please also see accompanying Medication Guide.
**Acthar® Gel**

**HIGHLIGHTS OF PRESCRIBING INFORMATION**

These highlights do not include all the information needed to use Acthar® Gel safely and effectively. See full prescribing information for Acthar Gel.

**Acthar Gel (repository corticotropin injection) INJECTION, GEL for INTRAMUSCULAR use**

Initial U.S. Approval: 1952

1. **INDICATIONS AND USAGE**

- Acthar Gel is indicated as monotherapy for the treatment of infantile spasms in infants and children under 2 years of age. (1.1)
- Acthar Gel is indicated for the treatment of exacerbations of multiple sclerosis in adults. (1.2)
- Acthar Gel may be used for the following disorders and diseases: rheumatic; collagen; dermatologic; allergic states; opthalmic; respiratory; and edematous state. (1.3 to 1.9)

2. **DOSAGE 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. (2.1)
- 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. (2.2)
- 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. (2.3)

3. **DOSE FORMS AND STRENGTHS**

- 5 mL multi-dose vial containing 80 USP units per mL. (3)

4. **CONTRAINDICATIONS**

- Acthar Gel should never be given intravenously.
- 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 Acthar Gel.
- 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)

5. **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)
- Elevated Blood Pressure, Salt and Water Retention and Hypokalemia: Monitor blood pressure and sodium and potassium levels. (5.3)
- Vaccination: Do not administer live or live attenuated vaccines to patients on immunosuppressive doses. (5.4)
- Masking of Symptoms of Other Underlying Disease/Disorders. Monitor patients for signs of other underlying disease/disorders that may be masked. (5.5)
- Gastrointestinal Perforation and Bleeding: There is a risk for gastric ulcers and bleeding. There is an increased risk of perforation in patients with certain GI disorders. Signs and symptoms may be masked. Monitor for signs of perforation and bleeding. (5.6)
- Behavioral and Mood Disturbances. May include euphoria, insomnia, mood swings, personality changes, severe depression and psychosis. Existing conditions may be aggravated. (5.7)
- Comorbid Diseases: Symptoms of diabetes and myasthenia gravis may be worsened with treatment. (5.8)
- Ophthalmic Effects: Monitor for cataracts, infections and glaucoma. (5.9)
- Immunogenicity Potential: Neutralizing antibodies with chronic administration may lead to a loss of endogenous ACTH activity. (5.10)
- Use in Patients with Hypothyroidism or Liver Cirrhosis: May result in an enhanced effect. (5.11)
- Negative Effects on Growth and Physical Development: Monitor pediatric patients on long term therapy. (5.12)
- Decrease in Bone Density: Monitor for osteoporosis in patients on long term therapy. (5.13)
- Use in Pregnancy: Embryocidal effect. Apprise women of potential harm to the fetus. (5.14)

6. **ADVERSE REACTIONS**

- Common adverse reactions for 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)
- Specific 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)

7. **DRUG INTERACTIONS**

- Acthar Gel may accentuate the electrolyte loss associated with diuretic therapy. (7)

8. **USE IN SPECIFIC POPULATIONS**

- Pregnancy: Acthar Gel 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. (8.1)
- Pediatric Use: Prolonged use of Acthar Gel in children may inhibit skeletal growth. If use is necessary, it should be given intermittently with careful observation. (5.12 and 8.4)

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

Revised: 3/2019

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**FULL PRESCRIBING INFORMATION: CONTENTS**

**FULL PRESCRIBING INFORMATION**

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   1.2 Multiple Sclerosis
   1.3 Rheumatic Disorders
   1.4 Collagen Diseases
   1.5 Dermatologic Diseases
   1.6 Allergic States
   1.7 Ophthalmic Diseases
   1.8 Respiratory Diseases
   1.9 Edematous State

2. **DOSAGE AND ADMINISTRATION**

   2.1 Specific Recommended Dosage Regimen for Infantile Spasms in Infants and Children Under 2 Years of Age
   2.2 Recommended Dosage Regimen for the Treatment of Acute Exacerbations in Adults with Multiple Sclerosis
   2.3 Recommended Dosage Regimen for Other Indications for Adults and Children Over 2 Years of Age
   2.4 Preparation

3. **DOSE FORMS AND STRENGTHS**

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9. **OVERDOSAGE**

10. **DESCRIPTION**

11. **CLINICAL PHARMACOLOGY**

12. **NONCLINICAL TOXICOLOGY**

13. **CLINICAL STUDIES**

14. **HOW SUPPLIED / STORAGE AND HANDLING**

15. **PATIENT COUNSELING INFORMATION**

*Sections or subsections omitted from the full prescribing information are not listed.
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 adenocortical insufficiency, adrenocortical hyperfunction or sensitivity to proteins of porcine origin.

5 Warnings and Precautions

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

5.1 Infections

Adrenal insufficiency may increase the risks related to infections with any pathogen, including viral, bacterial, fungal, protozoan or helminthic infections. Patients with latent tuberculous or tuberculin reactivity should be observed closely, and if therapy is prolonged, chemoprophylaxis should be instituted.

5.2 Cushing’s Syndrome and Adrenal Insufficiency Upon Withdrawal

Treatment with Acthar Gel can cause hypothalamic-pituitary-axis (HPA) suppression and Cushing’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, lethargy, weakness, excessive weight loss, hypotension and abdominal pain. It is critical that parents and caregivers be made aware of the possibility of adrenal insufficiency when discontinuing 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 Cushing’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

Acthar Gel can cause elevation of blood pressure, salt and water retention, and increased extracellular potassium concentration. 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 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 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

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, hypertension, hyperglycemia, change in body weight and fecal blood loss.

5.6 Gastrointestinal Perforation and Bleeding

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 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 Acthar Gel in patients with diabetes and myasthenia gravis.

5.9 Ophthalmic Effects

Prolonged use of 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

Acthar Gel is immunogenic. Limited available data suggest that a patient may develop antibodies to Acthar Gel after chronic administration and loss of endogenous ACTH and Acthar Gel activity. Prolonged administration of 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 Acthar Gel may have negative effects on growth and physical development in children. Changes in appetite are seen with Acthar Gel therapy, with the effects becoming more frequent as the dose or treatment period increases. These effects are reversible once 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. decreases 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
Acthar Gel has been shown to have an embryocidal effect. Apprise women of potential harm to the fetus [see Use in Specific Populations (8.1)].

6 ADVERSE REACTIONS

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
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.

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 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.

6.2 Postmarketing Experience

The following adverse reactions associated with the use of Acthar Gel have been identified from postmarketing experience with Acthar Gel. Only adverse events that are not listed above 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.

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.

6.2.1 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
Decreased 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.

6.2.7 Metabolic
Negative nitrogen balance due to protein catabolism.

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 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 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 Ophthalmologic
Exophthalmos.

6.3.7 Ophthalmic
Necrotizing angitis (adults only) and congestive heart failure.

7 DRUG INTERACTIONS
Formal drug-drug interaction studies have not been performed. Acthar Gel may accentuate the electrolyte loss associated with diuretic therapy.

8 USE IN SPECIFIC POPULATIONS

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

8.3 Nursing Mothers
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Acthar Gel, when treating a nursing mother, a decision should be made whether to discontinue nursing or to discontinue the drug, considering the risk and benefit to the mother.

#### TABLE: Incidence (%) of Treatment Emergent Adverse Events Occurring in ≥ 2% of 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 qd n=57 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertrophy</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Endocrine disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cushingoid</td>
<td>3</td>
<td>22</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Irritability</td>
<td>7</td>
<td>19</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection*</td>
<td>20</td>
<td>46</td>
</tr>
<tr>
<td>Investigations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight gain</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased appetite</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Convulsion†</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal Congestion</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acne</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>Rash</td>
<td>0</td>
<td>8</td>
</tr>
</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.
10 OVERDOSAGE
While chronic exposure to 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, will produce the potential for serious adverse effects compared to a standard dose. There have been no reports of death or acute overdose symptoms from Acthar Gel in clinical studies 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 Acthar Gel to treat an infant that has a BSA of 0.4 m² would be 60 U/day. Using the 1-cyrrine supplied with Acthar Gel, the maximum amount that can be injected is 80 Unirection, which is a well-tolerated single dose.

11 DESCRIPTION
Acthar Gel is a naturally sourced complex mixture of adrenocorticotropic hormone analogs and other pituitary peptides. The Acthar Gel manufacturing process converts the initial porcine pituitary extract 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 supplied as a sterile preparation in 16% gelatin to provide a prolonged release formulation. The clinically active component is the intact ACTH and other pituitary peptides. The Acthar Gel manufacturing process converts the initial porcine pituitary extract 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 also reported to bind to melanocortin receptors.

The trophic effects of endogenous ACTH and 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 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 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

 Adequate and well-controlled studies 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 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 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 spasms and hypsarrhythmia on a full sleep cycle video EEG performed 2 weeks after treatment initiation, rated by an investigator blinded to treatment. Thirteen of 15 patients (86.7%) responded to 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 to the prednisone treatment were eligible to receive Acthar Gel treatment. Seven of 8 patients (87.5%) responded to Acthar Gel after not responding to prednisone. Similarly, the 2 nonresponder patients from the Acthar Gel treatment were eligible to receive treatment with prednisone. One of the 2 patients (50%) responded to the prednisone treatment after not responding to Acthar Gel.

A supportive single-blind, randomized clinical trial comparing high-dose, long-duration treatment (150 U/m² once daily for 3 weeks, n=30) of Acthar Gel with low-dose, short-duration treatment (20 U once daily for 2 weeks, n=29) for the treatment of infantile spasms was also evaluated in infants and children less than 2 years of age. Nonresponders (defined as in the previously described study) in the low-dose group received a dose escalation at 2 weeks to 50 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 hypsarrhythmia.

16 HOW SUPPLIED / STORAGE AND HANDLING

Acthar Gel (repository corticotropin injection) is supplied as 5 mL multi-dose vial (63004-8710-1) containing 80 USP Units per mL. Acthar Gel (repository corticotropin injection) should be warmed to room temperature before using. Do not overpressurize the vial prior to withdrawing the product.

Store Acthar Gel (repository corticotropin injection) under refrigeration between 2° to 8°C (36° to 46°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 Acthar Gel. Patients should be instructed to take Acthar Gel only 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 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 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 infections to minimize the risk of infection while taking Acthar Gel [see Warnings and Precautions (5.1) and Adverse Reactions (6.1.1)].

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 (5.12) and Adverse Reactions (6.1.1)].

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 stopped. Since the recovery of the adrenal gland varies from days to months, 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 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 Acthar Gel [see Warnings and Precautions (5.2)].

Patients, their caregivers and families should be advised that prolonged use of Acthar Gel in children may result in Cushings’s syndrome and associated adverse reactions, may inhibit skeletal growth, and may cause osteoporosis and decreased bone density. If prolonged use is necessary, Acthar Gel should be given intermittently along with careful observation [see Warnings and Precautions (5.2), (5.12), and (5.13) and Adverse Reactions (6.1.1)].

Patients, their caregivers and families should be informed that 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 while using 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 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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