b) Draw baseline blood sample for cortisol determination and administer 0.5 Units/kg of ACTH gel IM. Draw sample 120 minutes after injection.

Normals: Pre-ACTH 1.1–8 micrograms/dl; Post-ACTH 6.2–16.8 micrograms/dl. Hyperadrenocorticism: Pre-ACTH 4–10.8 micrograms/dl; Post-ACTH 11.7–50 micrograms/dl.

Hypoadrenocorticism: Pre-ACTH and Post-ACTH: ≤ 1 micrograms/dl (Morgan 1988)

■ CATS:

ACTH Stimulation Test:

a) Draw baseline blood sample for cortisol determination and administer 2.2 Units/kg of ACTH gel IM. Draw samples at 60 minutes and 120 minutes after injection. (Peterson and Randolph 1989), (Kemppainen and Zerbe 1989b)

b) Draw baseline blood sample for cortisol determination and administer 0.5 Units/kg of ACTH gel IM. Draw sample 120 minutes after injection.

Normals: Pre-ACTH 0.33–2.6 micrograms/dl; Post-ACTH 4.8–7.6 micrograms/dl. Hyperadrenocorticism: Pre-ACTH 4–10.8 micrograms/dl; Post-ACTH 11.7–50 micrograms/dl.

Hypoadrenocorticism: Pre-ACTH and Post-ACTH: ≤ 1 micrograms/dl (Morgan 1988)

■ CATTLE:

For ACTH deficiency or for primary bovine ketosis:

a) 200–600 Units initially followed by daily or semi-daily dose of 200–300 Units (Package Insert; *Adrenomone®*—Summit Hill)

b) 200 Units IM daily (Howard 1986)

■ HORSES:

ACTH Stimulation Test:

a) Draw baseline blood sample for cortisol determination and administer 1 Unit/kg IM of ACTH gel. Draw second sample 8 hours later. Normal stimulation will result in serum cortisol levels will increase 2–3 times. Horses with pituitary tumors will increase cortisol fourfold after ACTH. (Beech 1987b)

b) Obtain pre-dose level. Administer 1 Unit/kg IM of ACTH gel between 8 and 10 AM; take post ACTH cortisol levels at 2 and 4 hours post dose. Horses with a functional adrenal gland should have a 2- to 3-fold increase in plasma cortisol when compared with baseline. (Toribio 2004a)

■ BIRDS:

ACTH Stimulation Test:

a) Draw baseline blood sample for corticosterone (not cortisol) determination and administer 16–25 Units IM. Draw second sample 1–2 hours later. Normal baseline corticosterone levels vary with regard to species, but generally range from 1.5–7 ng/mL. After ACTH, corticosterone levels generally increase by 5–10 times those of baseline. Specific values are listed in the reference. (Lothrop and Harrison 1986)

Chemistry/Synonyms

A 39 amino acid polypeptide, corticotropin is secreted from the anterior pituitary. The first 24 amino acids (from the N-terminal end of the chain) define its biologic activity. While human, sheep, cattle and swine corticotropin have different structures, the first 24 amino acids are the same and, therefore, biologic activity is thought to be identical. Commercial sources of ACTH have generally been obtained from porcine pituitaries. One USP unit of corticotropin is equivalent to 1 mg of the international standard.

Corticotropin may also be known as: ACTH, adrenocorticotrophic hormone, adrenocorticotrophin, corticotrophin, corticotropinum, *Acethropan®, Acortan simplex®, Actharn®, Acthelea®, Acton prolongatum®, H.P. Acthar®* or *Cortrophin-Zinc®*.

Storage/Stability/Compatibility

Corticotropin in the past has been available commercially as corticotropin for injection, repository corticotropin for injection, and corticotropin zinc hydroxide suspension. Corticotropin is commonly called ACTH (abbreviated from adrenocorticotropic hormone). Repository corticotropin is often called ACTH gel and is the most commonly used ACTH product in veterinary medicine.

Corticotropin for injection (aqueous) can be stored at room temperature (15–30°C) before reconstitution. After reconstitution, it should be refrigerated and used within 24 hours. Repository corticotropin injection should be stored in the refrigerator (2–8°C). To allow ease in withdrawing the gel into a syringe, the vial may be warmed with warm water prior to use.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

Compounded ACTH products may be available from compounding pharmacies.

HUMAN-LABELED PRODUCTS:

Corticotropin, Repository for Injection: 80 Units/mL in mL 5 mL multi-dose vials; *H.P. Acthar® Gel* (Questcor); (Rx) **Note:** This product is only available through a specialty pharmacy distribution system and is not available via regular retail pharmacies or drug wholesalers.

COSYNTROPIN

(koh-***sin***-troh-pin) Cortrosyn®, Synacthen®

HORMONAL DIAGNOSTIC AGENT

Prescriber Highlights

- Alternative to ACTH for adrenal function tests
- Drug-lab interactions
- Availability & expense have been issues

Uses/Indications

Cosyntropin is used primarily as an alternative to ACTH to test for adrenocortical insufficiency (Addison's), or hyperadrenocorticism, particularly in animals who have reacted immunologically to corticotropin in the past or if ACTH gel is unavailable.

Pharmacology/Actions

Like endogenous corticotropin, cosyntropin stimulates the adrenal cortex (in normal patients) to secrete cortisol, corticosterone, etc. Because of its structure, corticotropin is not as immunogenic as endogenous corticotropin. Apparently, the bulk of immunogenicity resides in the C-terminal portion of corticotropin (22–39 amino acids) and cosyntropin ends after amino acid #24.

Pharmacokinetics

Cosyntropin must be given parenterally because it is inactivated by gut enzymes. It is rapidly absorbed after being given IM. After giving IM or rapid IV, plasma cortisol levels reach their peak within an hour. It is unknown how cosyntropin is inactivated or eliminated.

Contraindications/Precautions/Warnings

Contraindicated in patients with known hypersensitivity to cosyntropin. Use caution in patients who have shown hypersensitive reactions to ACTH in the past; there is a distinct possibility that cross-reactivity could occur.

Adverse Effects

When used short-term, the only real concern is hypersensitivity reactions.

Reproductive/Nursing Safety

In humans, the FDA categorizes this drug as category ***C*** for use during pregnancy (*Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in humans; or there are no animal reproduction studies and no adequate studies in humans.*)

Overdosage/Acute Toxicity

Unlikely to be of clinical consequence if used one-time only.

Laboratory Considerations

- Patients should not receive **hydrocortisone** or **cortisone** on test day; dexamethasone sodium phosphate does not interfere with cortisol assays
- If using a fluorometric analysis: Falsely high values may be observed if the patient is taking **spironolactone**
- Falsely high values may be observed in patients with high **bilirubin** or if free plasma hemoglobin present

Doses

- **DOGS:**

  For testing (screening) adrenal function:

  a) For tentative diagnosis of Addison's disease: 1) Draw blood for hemogram, serum biochemistry and basal cortisol; 2) Begin IV fluids and give 2–5 mg/kg dexamethasone sodium phosphate; 3) Immediately give 0.25 mg of cosyntropin IV or IM; 4) Draw a second blood sample for plasma cortisol 45–60 minutes later. Blood levels of <1 mcg/dL are typical for hypoadrenocorticism, while those stimulating to only 2–3 mcg/dL are also suggestive. (Schaer 2006)

  b) 5 mcg/kg IV; measure serum cortisol at 0 and 1 hour. (Watson, Church et al. 1998)

  c) 5 mcg/kg with a maximum of 250 mcg IV. Once reconstituted, the solution may be frozen for up to six months and used. (Behrend 2003a)

  d) For ACTH Stimulation test: Two different protocols: 1 mcg/kg or 250 mcg/dog IV or IM with serum cortisol measured before and 1 hour post injection. 80–85% of dogs with pituitary-dependent hyperadrenocorticism (PD) and 60% of dogs with adrenal tumor/hyperplasia (AT) will have an exaggerated response. Unfortunately, just about any other extra-adrenal illness can cause an exaggerated post-ACTH level. (Reine 2006)

- **CATS:**

  For testing (screening) adrenal function:

  a) For tentative diagnosis of Addison's disease: 1) Draw blood for hemogram, serum biochemistry and basal cortisol; 2) Begin IV fluids and give 2–5 mg/kg dexamethasone sodium phosphate; 3) Immediately give 0.125 mg of cosyntropin IV or IM; 4) Draw a second blood sample for plasma cortisol 45–60 minutes later. Blood levels of <1 mcg/dL are typical for hypoadrenocorticism, while those stimulating to only 2–3 mcg/dL are also suggestive. (Schaer 2006)

  b) 0.125 mg (total dose—125 mcg) IM or IV. Begin test between 8–9 AM; obtain preinjection cortisol level and 30 minutes and 1 hour post. (Feldman 2000)

  c) For diagnosis of hyperadrenocorticism in cats: 125 mcg/cat IM or IV with cortisol measurements before and at 30 and 60 minutes post. (Reine 2006)

- **HORSES:**

  For testing (screening) adrenal function:

  a) For relative adrenal insufficiency (RIA) evaluation in critically ill horses: Draw blood for baseline cortisol and give cosyntropin at 0.1 mcg/kg; cortisol will peak after 30 minutes. (Stewart 2006)

  b) Obtain pre-dose level. Administer 1 mg IV of cosyntropin between 8 and 10 AM; take post ACTH cortisol levels at 2 hours post dose. Horses with a functional adrenal gland should have at least a two-fold increase in plasma cortisol when compared with baseline. (Toribio 2004a)

Monitoring

- See specific protocols for test procedures

Chemistry/Synonyms

A synthetic polypeptide that mimics the effects of corticotropin (ACTH), cosyntropin is commercially available as a lyophilized white to off-white powder containing mannitol. Cosyntropin's structure is identical to the first 24 (of 39) amino acids in natural corticotropin. 0.25 mg of cosyntropin is equivalent to 25 units of corticotropin.

Cosyntropin may also be known as: tetracosactide, alpha(1–24)-corticotrophin, beta(1–24)-corticotrophin, tetracosactido, tetracosactidum, tetracosactrin, tetracosapeptide, *Cortrosina®*, *Cortrosyn®*, *Nuvacthen Depot®*, *Synacthen®*, *Synacthen Depot®*, *Synacthen Retard®*, or *Synacthene®*.

Storage/Stability/Compatibility

After reconstituting with sterile normal saline, the solution is stable for 24 hours at room temperature; 21 days if refrigerated. Do not add the drug to blood or plasma infusions. One study (Frank and Oliver 1998) showed that cosyntropin can be reconstituted and stored frozen (-20°C) in plastic syringes for up to 6 months and still show biologic activity in the dog. It is recommended to freeze in small aliquots as it is unknown what effect thawing and refreezing has on potency.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Cosyntropin Powder for Injection: 0.25 mg lyophilized (250 mcg) in vials with 10 mg mannitol with diluent; *Cortrosyn®* (Amphastar); (Rx)