HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use COSYNTROPIN INJECTION safely and effectively. See full prescribing information for COSYNTROPIN INJECTION.

COSYNTROPIN injection, for intravenous use
Initial U.S. Approval: 2008

---------- INDICATIONS AND USAGE ----------

Cosyntropin Injection is an adrenocorticotropic hormone indicated in combination with other diagnostic tests, for use as a diagnostic agent in the screening of adrenocortical insufficiency in adults and pediatric patients. (1)

---------- DOSAGE AND ADMINISTRATION ----------

- In general, stop glucocorticoids and spironolactone on the day of cosyntropin testing. For long-acting glucocorticoids, stop for a longer period before cosyntropin testing. (2.1)
- For adults, the recommended dose is 0.25 mg to be administered by intravenous injection. (2.2)
- For pediatric patients, the recommended dose to be administered by intravenous injection is (2.3):
  - 0.125 mg for patients birth to less than 2 years of age
  - 0.25 mg for patients 2 to 17 years of age
- Obtain blood samples for serum cortisol level at baseline and exactly 30 and 60 minutes after cosyntropin administration. (2.4)
- See Full Prescribing Information for interpretation of cortisol levels information (2.5)

---------- DOSAGE FORMS AND STRENGTHS ----------

- Injection: 0.25 mg/mL of cosyntropin in 1 mL single-dose vial (3)

---------- CONTRAINDICATIONS ----------

- Cosyntropin Injection is contraindicated in patients with a history of hypersensitivity to cosyntropin or to any excipients of Cosyntropin Injection. Reactions have included anaphylaxis. (4, 5.1)

---------- WARNINGS AND PRECAUTIONS ----------

- *Hypersensitivity*: reactions including anaphylaxis have been reported. Monitor patients for hypersensitivity reactions and treat as needed. (5.1)
- *Diagnostic Inaccuracies*: Cortisol levels and subsequent diagnosis of adrenocortical insufficiency following Cosyntropin Injection administration may be inaccurate if patients are on certain medications because of their effect on cortisol binding globulin levels. Any condition that elevates or lowers cortisol binding globulin levels may increase or decrease plasma total cortisol levels, respectively. (2.1, 5.2, 7)

---------- ADVERSE REACTIONS ----------

Most common adverse reactions are: anaphylactic reaction, bradycardia, tachycardia, hypertension, peripheral edema, and rash (6)

To report SUSPECTED ADVERSE REACTIONS, contact Sandoz Inc., at 1-800-525-8747 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- DRUG INTERACTIONS ----------

- Drug effects on plasma cortisol levels:
  - Accuracy of the test results can be affected by concomitant medications.
  - Glucocorticoids and spironolactone: May falsely elevate plasma cortisol levels. Stop these drugs on day of Cosyntropin Injection testing. Long-acting glucocorticoids may need to be stopped for a longer period before Cosyntropin Injection testing. (7)
  - Estrogen: May elevate plasma total cortisol levels. Stop estrogen containing drugs 4 to 6 weeks before Cosyntropin Injection testing. (7)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 07/2024

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Cosyntropin Injection is indicated, in combination with other diagnostic tests, for use as a diagnostic drug in the screening of adrenocortical insufficiency in adults and pediatric patients

2 DOSAGE AND ADMINISTRATION

2.1 Important Information Before Conducting Cosyntropin Injection Testing

- In general, stop glucocorticoids and spironolactone on the day of Cosyntropin testing. However, long-acting glucocorticoids may need to be stopped for a longer period before Cosyntropin testing *[see Warnings and Precautions (5.2), Drug Interactions (7)]*.
- Stop estrogen-containing drugs four to six weeks before Cosyntropin testing *[see Warnings and Precautions (5.2), Drug Interactions (7)]*.

2.2 Recommended Dose for Adults

- The recommended dose of Cosyntropin Injection in adults is 0.25 mg to be administered by intravenous injection.

2.3 Recommended Dose for Pediatric Patients

- The recommended dose of Cosyntropin Injection in pediatric patients, aged birth to 17 years, to be administered by intravenous injection is presented in Table 1.

Table 1: Recommended Cosyntropin Dose for Pediatric Patients

Age	Recommended Dose	Volume of Solution
Birth to less than 2 years	0.125 mg	0.5 mL
2 to 17 years	0.25 mg	1 mL

2.4 Administration Information

- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Only use if the solution is clear and colorless.
- Obtain blood sample for baseline serum cortisol. Obtain blood samples for assessment of cortisol levels exactly 30 minutes and 60 minutes after administration of Cosyntropin Injection.
- Discard any unused portion.
- Do not administer Cosyntropin Injection intramuscularly.

2.5 Interpretation of Plasma Cortisol Levels After Cosyntropin Injection

Stimulated plasma cortisol levels of less than 18 mcg/dL at 30- or 60-minutes post-Cosyntropin Injection are suggestive of adrenocortical insufficiency. Cutoff values for exclusion of adrenal insufficiency may vary according to the assay used. Test results can be affected by concomitant medications and certain medical conditions *[see Warnings and Precautions (5.2)]*.

3 DOSAGE FORMS AND STRENGTHS

Injection: 0.25 mg/mL is a clear, colorless solution in a 1 mL single-dose vial.

4 CONTRAINDICATIONS

Cosyntropin Injection is contraindicated in patients with a history of a hypersensitivity to cosyntropin or, synthetic ACTH, or to any excipients of Cosyntropin Injection. Reactions have included anaphylaxis *[see Warnings and Precautions (5.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity to Cosyntropin Injection

Cosyntropin injection hypersensitivity reactions including anaphylaxis have been reported. Monitor patients for hypersensitivity reactions and treat as needed.

5.2 Diagnostic Inaccuracies

Cortisol levels and subsequent diagnosis of adrenocortical insufficiency following Cosyntropin Injection administration may be inaccurate if patients are on certain medications because of their effect on cortisol binding globulins.

Glucocorticoids and spironolactone may result in falsely elevated cortisol levels. Stop these drugs on the day of cosyntropin testing. Long-acting glucocorticoids may need to be stopped for a longer period before cosyntropin testing *[see Dosage and Administration (2.1) and Drug Interactions (7)]*.

Estrogen-containing drugs increases cortisol binding globulin levels which can increase plasma total cortisol levels. To obtain accurate plasma total cortisol levels, stop estrogen-containing drugs four to six weeks before cosyntropin testing to allow cortisol binding globulin levels to return to levels within the reference range *[see Dosage and Administration (2.1) and Drug Interactions (7)]*. Alternatively, concomitant measurement of cortisol binding globulin at the time of testing can be done; if cortisol binding globulin levels are elevated, plasma total cortisol levels are considered inaccurate.

Any condition that elevates or lowers cortisol binding globulin levels may increase or decrease plasma total cortisol levels, respectively. Cortisol binding globulin levels can be low in cirrhosis or nephrotic syndrome. Measure cortisol binding globulin levels is recommended to ensure accuracy of interpretation of plasma total cortisol levels.

6 ADVERSE REACTIONS

The following serious adverse reactions are described below and elsewhere in the labeling:

- Hypersensitivity Reactions *[see Warnings and Precautions (5.1)]*
- Diagnostic Inaccuracies *[see Warnings and Precautions (5.2)]*

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. The following adverse reactions have been identified during post-approval use of cosyntropin:

- anaphylactic reaction
- bradycardia
- tachycardia
- hypertension
- peripheral edema
- rash

7 DRUG INTERACTIONS

7.1 Drug Effects on Plasma Cortisol Levels

- Accuracy of diagnosis can be complicated by concomitant medications. Plasma cortisol levels and subsequent diagnosis of adrenocortical insufficiency following Cosyntropin Injection administration may be inaccurate if patients are on certain medications because of their effect on cortisol or cortisol binding globulin levels *[see Dosage and Administration (2.1) and Warnings and Precautions (5.2)]*.

- Glucocorticoids and spironolactone may falsely elevate plasma cortisol levels. Stop these drugs on the day of Cosyntropin Injection testing. Long-acting glucocorticoids may need to be stopped for a longer period before Cosyntropin Injection testing.
- Estrogen: May elevate plasma total cortisol levels. Discontinue estrogen containing drugs 4 to 6 weeks prior to testing to allow cortisol binding globulin levels to return to levels within the reference range. Alternatively, concomitant measurement of cortisol binding globulin at the time of testing can be done; if cortisol binding globulin levels are elevated, plasma total cortisol levels are considered inaccurate.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available data from case reports over decades of use with cosyntropin during pregnancy have not identified an increased risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Unidentified adrenal insufficiency can result in adverse maternal or fetal outcomes *(see Clinical Considerations)*.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk for major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease-associated maternal and/or embryo/fetal risk
Unidentified adrenal insufficiency during pregnancy can result in maternal and/or fetal death; therefore, the diagnosis of suspected adrenal insufficiency during pregnancy should not be delayed.

8.2 Lactation

Risk Summary

There are no data on the presence of cosyntropin in human milk, the effects on the breastfed infant, or the effects on milk production. The development and health benefits of breastfeeding should be considered along with the mother's clinical need for Cosyntropin Injection and any potential adverse effects on the breastfed infant from Cosyntropin Injection or from the underlying maternal condition.

8.4 Pediatric Use

Cosyntropin Injection is approved for use in pediatric patients *[see Dosage and Administration (2.3)]*

11 DESCRIPTION

Cosyntropin, an adrenocorticotropic hormone analog for intravenous use, is α 1-24 corticotropin, a synthetic subunit of ACTH. It is an open chain polypeptide with a molecular weight of 2933.44 containing, from the N terminus, the first 24 of the 39 amino acids of natural ACTH. The molecular formula of Cosyntropin is $C_{136}H_{210}N_{40}O_{31}S$. Its amino acid sequence is as follows:

Ser -	Tyr -	Ser -	Met -	Glu -	His -	Phe -	Arg -	Trp -	Gly -	Lys -	Pro -
1	2	3	4	5	6	7	8	9	10	11	12
Val -	Gly -	Lys -	Lys -	Arg -	Arg -	Pro -	Val -	Lys -	Val -	Tyr -	Pro
13	14	15	16	17	18	19	20	21	22	23	24

Cosyntropin injection is a 1 mL sterile solution in single-dose vials containing 0.25 mg of cosyntropin as active, 0.82 mg sodium acetate trihydrate USP and 1 mg glacial acetic acid USP as buffering agent, 6.4 mg sodium chloride and 10 mg mannitol as tonicity adjustor and water for injection USP. Cosyntropin injection is a clear, colorless solution with a pH between 3.8 and 4.5.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Cosyntropin exhibits the full corticosteroidogenic activity of natural ACTH. Various studies have shown that the biologic activity of ACTH resides in the N-terminal portion of the molecule and that the 1-20 amino acid residue is the minimal sequence retaining full activity. Partial or complete loss of activity is noted with progressive shortening of the chain beyond 20 amino acid residues. For example, the decrement from 20 to 19 results in a 70% loss of potency.

The pharmacologic profile of cosyntropin injection is similar to that of purified natural ACTH. It has been established that 0.25 mg of cosyntropin injection will stimulate the adrenal cortex maximally and to the same extent as 25 units of natural ACTH. This dose of cosyntropin injection will produce maximal secretion of 17-OH corticosteroids, 17-ketosteroids and/or 17-ketogenic steroids.

12.2 Pharmacodynamics

The exposure-response relationship and time course of pharmacodynamic response for the safety and effectiveness of Cosyntropin Injection have not been fully characterized.

12.3 Pharmacokinetics

In a study in normal volunteers, plasma cortisol levels peaked about 2.5 ± 0.5 hours after intravenous injection of Cosyntropin and returned to baseline values by 6 hours.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term carcinogenicity studies in animals to evaluate the carcinogenic potential of cosyntropin have not been conducted. Studies to evaluate the mutagenic potential or impairment of fertility in animals have not been conducted.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

Cosyntropin injection is supplied in a single-dose amber vial containing 1 mL of clear, colorless, sterile solution.

NDC 0781-3052-95 Cosyntropin injection 0.25 mg/mL, Box of 10 x 1 mL single-dose vials

Storage and Handling

Store refrigerated between 2° to 8°C (36° to 46°F). Protect from light. Protect from freezing.

Cosyntropin Injection is intended as a single dose injection and contains no antimicrobial preservative. Any unused portion should be discarded.

17 PATIENT COUNSELING INFORMATION

Hypersensitivity Reactions, including Anaphylaxis

Inform patients and/or caregivers of the early signs of hypersensitivity reactions including rash, hives, itching, facial swelling, tightness of the chest, and wheezing *[see Contraindications (4) and Warnings and Precautions (5.1)]*.

Drug Interference with Cosyntropin Injection Testing

Advise patients and/or caregivers to stop taking glucocorticoids and spironolactone on the day of Cosyntropin Injection testing. However, for patients taking long-acting glucocorticoids, advise them to stop for longer periods before Cosyntropin Injection testing. Advise patients to stop taking estrogen-containing drugs four to six weeks before Cosyntropin Injection testing *[see Dosage and Administration (2.1), Warnings and Precautions (5.2), and Drug Interactions (7)]*.

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