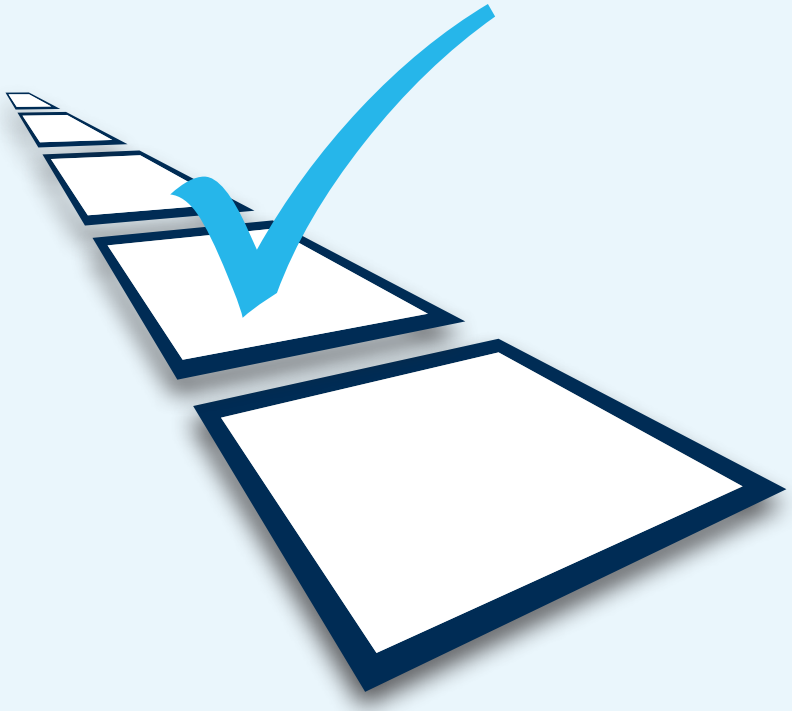
Synacthen®
TETRACOSACTIDE

Synacthen®



Synacthen®
TETRACOSACTIDE

Synacthen®

Tetracosactide

- Synthetic ACTH analogue [1]
- Corticotropin 1-24

Pack appearance may vary by country

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HPA axis

Hypothalamus - Pituitary - Adrenal (HPA) axis

Enable the body to cope with stresses [2] e.g.

- Infection
- Hypotension
- Surgery

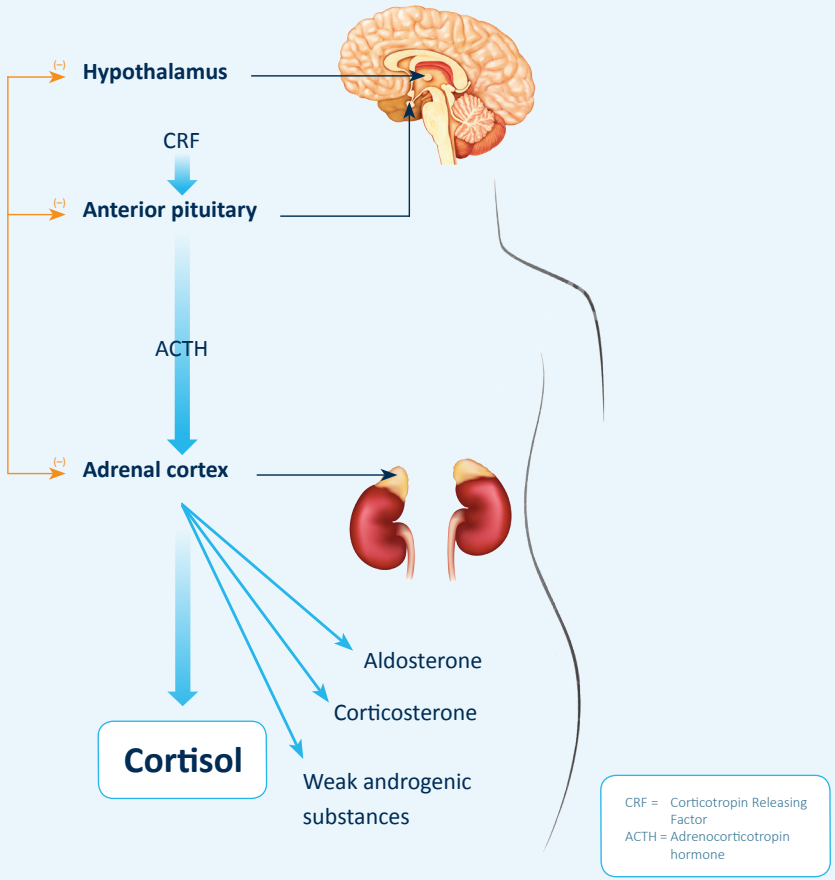
Adrenal deficiency may arise due to [3]

- Structural damage to adrenal gland
- Structural damage to pituitary gland
- Structural damage to hypothalamus

Most common cause of ACTH deficiency

- Prolonged administration of steroids [4]

The hypothalamic-pituitary-adrenocortical (HPA) axis



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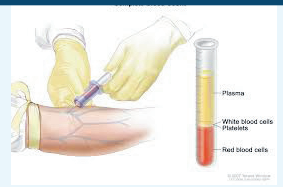
Synacthen® Test

Response to acute ACTH stimulation [7]

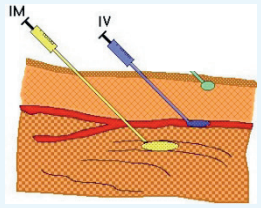
- A normal response is a rise in plasma cortisol levels after 30 minutes
- An impaired response confirms adrenal insufficiency

Highly predictive and sensitive test [5,6,9]

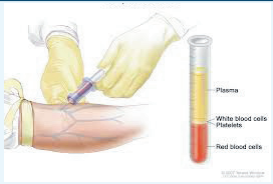
Collect plasma sample



Administer 250 mcg/ml Synacthen®
intravenously or intramuscularly



30 mins later take 2nd plasma sample



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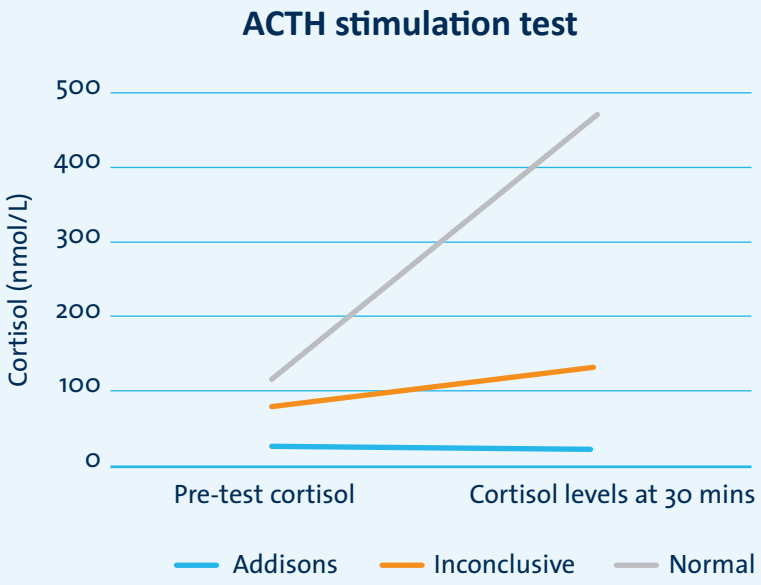
Interpreting the Diagnostic Test at 30 minutes [7]

- **Plasma cortisol increment**
  - Normal if the rise in plasma cortisol concentration > 200 nmol/L (70 mcg/L)
- **Absolute plasma cortisol**
  - Normal if the plasma cortisol concentration > 500 nmol/L (180 mcg/L)

- Where the test has yielded inconclusive results a 5-hour test can be performed with Synacthen® Depot



A normal response, a response consistent with Addison's disease and an inconclusive response are shown

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Factors which can influence the results of the Synacthen® Test [5]

- Pituitary surgery/trauma within previous 2 weeks [6]
- Exposure to steroid treatment (> 3weeks) [4]
  - > 300 mg hydrocortisone
  - 7.5 mg prednisolone
  - 0.75 mg dexamethasone
- Assay variability [5]

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Facts & Dosing [7] with Synacthen®

- Synacthen® is administered intramuscularly or intravenously
- Synacthen® should be stored in the refrigerator (2° to 8°C)
- Ampoule presentation containing 1 ml (250 mcg) tetracosactide

	Synacthen® Dosing
Adult	• 250 micrograms (1 ml) • i.m. or i.v. administration
Children	• Dose for children based on body surface area (BSA) • 250 micrograms/1.73 m^2 BSA i.v. administration • Aged 5-7 years, approx. half the adult dose

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Side-effect profile

Synacthen® Ampoules 250 mcg/ml

- Established safety profile demonstrated over decades [8]
- Side effects associated with increased output of mineralo- & gluco-corticoids may be encountered

Side effects associated with tetracosactide: [7]

- Hypersensitivity
- Adrenal haemorrhage

System/organ side effects related to corticoid effects (frequency not known) [7]

Infections and infestations
Blood and the lymphatic system disorders
Endocrine disorders
Metabolism and nutrition disorders
Psychiatric disorders
Nervous system disorders
Eye disorders
Cardiac disorders
Vascular disorders
Gastrointestinal disorders
Skin and subcutaneous tissue disorders
Musculoskeletal and connective tissue disorders
General disorders and administration site conditions
Investigations

Synacthen®

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Abbreviated Prescribing Information for Synacthen® Ampoules 250 mcg/ml [7]

Presentation: Each ampoule contains 250 mcg of Tetracosactide acetate

Indications: Diagnostic test for the investigation of adrenocortical insufficiency.

Dosage and Administration: For diagnostic purposes only as a single intramuscular or intravenous dose. Not to be used for repeated therapeutic administration

Adults and Elderly: For the 30-min Synacthen® diagnostic test: 250 micrograms (1ml) of Synacthen® is given via intramuscular or intravenous injection and blood sampling is performed before and 30-min after Synacthen® injection.

Please see Synacthen® SPC for full directions on carrying out diagnostic test.

Children: Suggested intravenous dose of 250 micrograms/1.73 m^2 body surface area.

Contraindications: Hypersensitivity to tetracosactide and/or ACTH or to any of the excipients. In patients with allergic disorders (e.g. asthma,) acute psychosis, infectious diseases, peptic ulcer, refractory heart failure, Cushing's syndrome, treatment of primary adrenocortical insufficiency and adrenocongenital syndrome.

Warnings and precautions: Exclude allergic conditions or history of adverse reaction to ACTH, Synacthen® or other drugs. Administer under the supervision of appropriate senior hospital medical staff. Observe for 30 minutes after injection for signs of hypersensitivity. If local or systemic reactions occur, discontinue Synacthen® or other ACTH preparation, treat patient appropriately and avoid products in the future. Not to be used in presence of active infection, with live vaccine or in reduced immune response unless adequate disease specific therapy is being given. Use with caution in patients with ulcerative colitis, diverticulitis, recent intestinal anastomosis, kidney failure, hypertension, predisposition to thromboembolism, osteoporosis, myasthenia gravis, ocular herpes simplex.

Increased production of adrenal steroids may result in corticosteroid type effects and there may be a need for dose adjustment in patients with diabetes or hypertension.

Contains less than 1 mmol sodium (23 mg) per ampoule.

Lack of diagnostic accuracy: Patients on oral contraceptives, post-operative patients, critical illness, severe liver disease, nephrotic syndrome may cause misleading post administration total plasma cortisol levels during Synacthen® Test. Assess the integrity of HPA axis using alternate parameters

Interactions: Valproate in pediatrics (may cause severe jaundice: avoid), Anticonvulsants (increased risk of liver damage; use Synacthen® Depot at minimum dose/duration), Endogenous and synthetic oestrogens (may affect results of diagnostic test), Adjust medication dosing for patients with diabetes mellitus or for moderate to severe hypertension when Synacthen® is started

Undesirable effects: Relating to tetracosactide: hypersensitivity and adrenal haemorrhage. Other side effects relating to glucocorticoid and mineralocorticoid effects. Please see the Synacthen® 250 mcg/ml Ampoules SPC for a full listing of effects.

Marketing authorisation holder: Questcor Operations Limited, 70 Sir John Rogerson's Quay, Dublin 2, Ireland.

Product authorisation number: PL43357/0001

For further information please contact: Questcor Operations Ltd, Sandyford Business Center, Unit 7, Dublin 18, Ireland. Telephone: 0035312902501 Email: SynacthenMedinfo@mallinckrodt.com

References: 1. Data on file: Synacthen® Depot Core Data Sheet, 2014; 2. Chatha et al, J Clin Biochem 2010; 47:158; 3. Marik et al, Crit Care 2008; 36(6):1937; 4. Cooper & Stewart, Rev Endo Metab Dis 2005; 6:47; 5. Agha et al, J Clin Endocrinol Metab 2006; 91(1):43; 6. Davies & Howlett J Royal Soc Med 1996; 89:159P; 7. Synacthen® Ampoules 250 mcg/ml SPC UK, Sep 2014; 8. PSUR No 7; 01 Jun 2008 – 31 May 2011; 9. Gleeson et al 2003

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