Withdrawal
Corticotropin use may depress the hypothalamic-pituitary-adrenal axis. Abrupt withdrawal of corticotropin may therefore produce adrenocortical and pituitary unresponsiveness, and therapy should be stopped gradually. An increase in corticosteroid requirements associated with the stress of infection, or accidental or surgical trauma, may also precipitate acute adrenocortical insufficiency. See also Withdrawal under Corticosteroids, p.1493.

Precautions
As for Corticosteroids, p.1493.

Phaeochromocytoma. A hypertensive crisis in a patient given intravenous tetracosactide led to the discovery of an adrenaline-secreting phaeochromocytoma in a patient.[1] It was suggested that caution should be observed when using corticotropin in patients with orthostatic hypotension in whom the diagnosis of phaeochromocytoma has not been excluded.

1. Jan T, *et al*. Epinephrine-producing pheochromocytoma with hypertensive crisis after corticotropin injection. *Am J Med* 1990; **89:** 824–5.

Interactions
Interactions seen with corticotropin are liable to be similar to those with corticosteroids (p.1494).

Uses and Administration
Corticotropin is a naturally occurring hormone of the anterior lobe of the pituitary gland. It stimulates the adrenal glands to secrete adrenocortical hormones, especially cortisol (hydrocortisone), some mineralocorticoids such as corticosterone, and, to a lesser extent, androgens. It has little effect on aldosterone secretion, which proceeds independently.

Secretion of corticotropin by the functioning pituitary gland is controlled by the release of corticorelin from the hypothalamus and is also regulated by a negative feedback mechanism involving concentrations of circulating glucocorticoids. Conditions of stress may also stimulate secretion.

Corticotropin may be used diagnostically to investigate adrenocortical insufficiency. It has also been used therapeutically in most of the conditions (with the exception of the adrenal deficiency states and adrenocortical overactivity) for which systemic corticosteroid therapy is indicated (p.1495). Such use is now fairly limited. However, corticotropin may be used in certain neurological disorders such as infantile spasms and multiple sclerosis. The synthetic polypeptide tetracosactide (p.1543), which has the same amino-acid sequence as the first 24 residues of human corticotropin, may be used as an alternative. Tosactide is another polypeptide analogue of corticotropin; it has the same sequence as the first 28 residues.

Corticotropin has been available for injection in two forms. One form is a plain injection that may be given by the subcutaneous, intramuscular, or intravenous routes. The other form is a long-acting depot preparation in which the viscosity is increased by the addition of gelatin, and which is given subcutaneously or intramuscularly; it must not be given intravenously. Individual responses to therapeutic corticotropin vary considerably and doses must be adjusted accordingly.

For *diagnostic purposes* the corticotropin test is based on the measurement of plasma-cortisol concentrations before and after injection. The plain preparation is used in doses of 10 to 25 units in 500 mL of glucose 5% infused intravenously over 8 hours.

For *therapeutic purposes* typical initial doses for the depot preparation have been about 20 to 80 units every 24 to 72 hours by the subcutaneous or the intramuscular route. As soon as possible the dosage should be reduced gradually to the minimum necessary to control symptoms.

A depot preparation of corticotropin combined with zinc hydroxide for intramuscular injection has been used in the past.

Epilepsy. The use of corticotropin in the management of infantile spasms is referred to under Epilepsy in Corticosteroids, p.1503.

Multiple sclerosis. Short-term courses of corticotropin have been used to speed recovery from acute exacerbations of multiple sclerosis (p.892) but corticosteroids, usually methylprednisolone, are now preferred.

Post-dural puncture headache. There are anecdotal reports of the relief of post-dural puncture headache by corticotropin or tetracosactide, but a controlled study of tetracosactide use found no benefit (see p.1544).

Preparations
USP 31: Corticotropin for Injection; Corticotropin Injection; Corticotropin Zinc Hydroxide Injectable Suspension; Repository Corticotropin Injection.

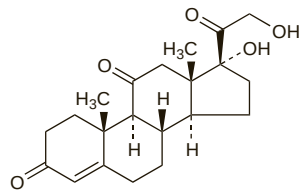
Proprietary Preparations (details are given in Part 3)
Arg.: Acthelea; ***Irl.:*** Acthar†; ***USA:*** Acthar.

Cortisone Acetate *(BANM, rINNM)* ⊗

Acetato de cortisona; Compound E Acetate; Cortisone, acétate de; Cortisoni acetas; 11-Dehydro-17-hydroxycorticosterone Acetate; Kortisonacetat; Kortison-acetát; Kortisoniasetaatti; Kortizon-acetát; Kortizono acetatas; Kortyzonu octan. 17α,21-Dihydroxypregn-4-ene-3,11,20-trione 21-acetate.

Кортизона Ацетат

$C_{23}H_{30}O_6$ = 402.5.
CAS — 53-06-5 (cortisone); 50-04-4 (cortisone acetate).
ATC — H02AB10; S01BA03.
ATC Vet — QH02AB10; QS01BA03.



(cortisone)

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, *US*, and *Viet.*
Ph. Eur. 6.2 (Cortisone Acetate). A white or almost white, crystalline powder. It shows polymorphism. Practically insoluble in water; slightly soluble in alcohol and in methyl alcohol; sparingly soluble in acetone; freely soluble in dichloromethane; soluble in dioxan. Protect from light.
USP 31 (Cortisone Acetate). A white or practically white, odourless, crystalline powder. Insoluble in water; soluble 1 in 350 of alcohol, 1 in 75 of acetone, 1 in 4 of chloroform, and 1 in 30 of dioxan. Store at a temperature of 25°, excursions permitted between 15° and 30°.

Adverse Effects, Treatment, Withdrawal, and Precautions
As for corticosteroids in general (see p.1490).

Interactions
The interactions of corticosteroids in general are described on p.1494.

Pharmacokinetics
For a brief outline of the pharmacokinetics of corticosteroids, see p.1495.

Cortisone acetate is readily absorbed from the gastrointestinal tract and the cortisone is rapidly converted in the liver to its active metabolite, hydrocortisone (cortisol). The biological half-life of cortisone itself is only about 30 minutes. Absorption of cortisone acetate from intramuscular sites is considerably slower than after oral doses.

Uses and Administration
Cortisone is a corticosteroid secreted by the adrenal cortex. It has glucocorticoid activity (p.1490), as well as appreciable mineralocorticoid activity; 25 mg of cortisone acetate is equivalent in anti-inflammatory activity to about 5 mg of prednisolone.

Cortisone acetate is rapidly effective when given orally, and more slowly by intramuscular injection.

Cortisone acetate has been used mainly for replacement therapy in adrenocortical insufficiency (p.1498), but hydrocortisone (p.1535) is generally preferred since cortisone itself is inactive and must be converted by the liver to hydrocortisone, its active metabolite; hence, in some liver disorders the activity of cortisone may be less reliable. Doses of cortisone acetate for oral replacement therapy are 12.5 to 37.5 mg daily in divided doses, with fludrocortisone if additional mineralocorticoid activity is required.

Cortisone acetate has been used in the treatment of many of the allergic and inflammatory disorders for which corticosteroid therapy is helpful (p.1495) but prednisolone or other synthetic glucocorticoids are generally preferred. Doses of cortisone acetate employed have generally ranged from about 25 to 300 mg daily by mouth or by intramuscular injection.

Preparations
BP 2008: Cortisone Tablets;
USP 31: Cortisone Acetate Injectable Suspension; Cortisone Acetate Tablets.

Proprietary Preparations (details are given in Part 3)
Austral.: Cortate; ***Belg.:*** Adreson†; ***Canad.:*** Cortone†; ***Ital.:*** Cortone; ***Neth.:*** Adreson†; ***S.Afr.:*** Cortogen†; ***UK:*** Cortisyl; ***USA:*** Cortone.

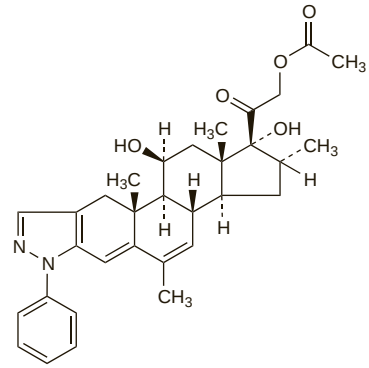
Multi-ingredient: ***Braz.:*** Corciclen; ***Spain:*** Blefarida; Gingilone.

Cortivazol *(USAN, pINN)* ⊗

Cortivazolum; H-3625; MK-650; NSC-80998. 11β,17α,21-Trihydroxy-6,16α-dimethyl-2′-phenyl-2′*H*-pregna-2,4,6-trieno[3,2-*c*]pyrazol-20-one 21-acetate.

Кортивазол

$C_{32}H_{38}N_2O_5$ = 530.7.
CAS — 1110-40-3.
ATC — H02AB17.
ATC Vet — QH02AB17.



Profile
Cortivazol is a corticosteroid with mainly glucocorticoid activity (p.1490); 300 micrograms of cortivazol is equivalent in anti-inflammatory activity to about 5 mg of prednisolone. It is given in the treatment of musculoskeletal and joint disorders by intra-articular, periarticular, or epidural injection in doses of about 1.25 to 3.75 mg, according to the size of the joint, usually at intervals of 1 to 3 weeks. It has also been given by mouth.

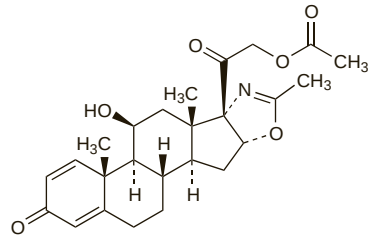
Preparations
Proprietary Preparations (details are given in Part 3)
Fr.: Altim.

Deflazacort *(BAN, USAN, rINN)* ⊗

Azacort; Deflatsakorti; Déflazacort; Deflazacortum; Deflazakort; DL-458-IT; L-5458; MDL-458; Oxazacort. 11β,21-Dihydroxy-2′-methyl-5′β*H*-pregna-1,4-dieno[17,16-*d*]oxazole-3,20-dione 21-acetate.

Дефлазакорт

$C_{25}H_{31}NO_6$ = 441.5.
CAS — 14484-47-0.
ATC — H02AB13.
ATC Vet — QH02AB13.



Profile
Deflazacort is a corticosteroid with mainly glucocorticoid activity (p.1490); 6 mg of deflazacort is reportedly equivalent in anti-inflammatory activity to about 5 mg of prednisolone (but see Action, below).

Deflazacort is used for its anti-inflammatory and immunosuppressant properties in conditions responsive to corticosteroid therapy (p.1495). It is given in initial oral doses of up to 120 mg