Dexamethasone

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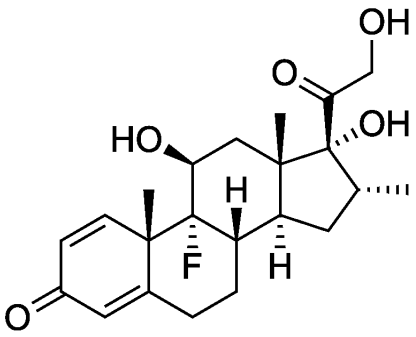
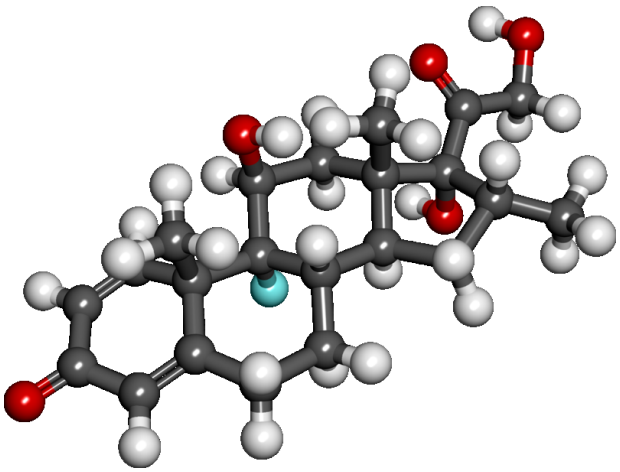




Systematic (IUPAC) name	
(8*S*,9*R*,10*S*,11*S*,13*S*,14*S*,16*R*,17*R*)-9- Fluoro-11,17-dihydroxy-17-(2-hydroxyacetyl)-10,13,16-trimethyl-6,7,8,9,10,11,12,13,14,15,16,17- dodecahydro-3*H*-cyclopenta[*a*]phenanthren-3-one	
Identifiers	
CAS number	50-02-2 [1]
ATC code	A01 AC02 [2] C05 AA09 [3], D07 AB19 [4], H02 AB02 [5], R01 AD03 [6], S01 BA01 [7], S02 BA06 [8], S03 BA01 [9]
PubChem	CID 5743 [10]
DrugBank	APRD00674 [11]
ChemSpider	5541 [12] ✓
UNII	7S5I7G3JQL [13] ✓
KEGG	D00292 [14] ✓
ChEMBL	CHEMBL384467 [15] ✓
Chemical data	
Formula	$C_{22}H_{29}FO_5$
Mol. mass	392.461 g/mol

SMILES	eMolecules [16] & PubChem [17]
Pharmacokinetic data	
Bioavailability	80-90%
Protein binding	70%
Metabolism	hepatic
Half-life	36-54 hours
Excretion	renal
Therapeutic considerations	
Pregnancy cat.	C(US)
Legal status	℞ Prescription only
Routes	Oral, IV, IM, SC and IO
✓ **(what is this?) (verify)** [18]	

Dexamethasone is a potent synthetic member of the glucocorticoid class of steroid drugs. It acts as an anti-inflammatory and immunosuppressant. It is 20 to 30 times more potent than the naturally occurring hormone cortisol and 4 to 5 times more potent than prednisone.

Therapeutic use

Anti-inflammatory

Dexamethasone is used to treat many inflammatory and autoimmune conditions, such as rheumatoid arthritis.

It is also given in small amounts[19] (usually 5-6 tablets) before and/or after some forms of dental surgery, such as the extraction of the wisdom teeth, an operation which often leaves the patient with puffy, swollen cheeks.

It is injected into the heel when treating plantar fasciitis, sometimes in conjunction with triamcinolone acetonide.

It is useful to counteract allergic anaphylactic shock, if given in high doses. It is present in certain eye drops – particularly post-eye surgery drops – and as a nasal spray (trade name Dexacort), and certain ear drops (Sofradex, when combined with an antibiotic and an antifungal).

Dexamethasone is used in transvenous screw-in cardiac pacing leads to minimize the inflammatory response of the myocardium. The steroid is released into the myocardium as soon as the screw is extended and can play a significant role in minimizing the acute pacing threshold due to the reduction of inflammatory response. The typical quantity present in a lead tip is less than 1.0 mg.

Dexamethasone is often administered before antibiotics in cases of bacterial meningitis. It then acts to reduce the inflammatory response of the body to the bacteria killed by the antibiotics (bacterial death releases pro-inflammatory mediators that can cause a response which is harmful to the patient), thus improving prognosis and outcome.[20]

Oncologic uses

Cancer patients undergoing chemotherapy are given Dexamethasone to counteract certain side-effects of their antitumor treatment. Dexamethasone can augment the antiemetic effect of 5-HT_3 receptor antagonists like ondansetron. In brain tumours (primary or metastatic), dexamethasone is used to counteract the development of edema, which could eventually compress other brain structures. Dexamethasone is also given in cord compression where a tumor is compressing the spinal cord.

Dexamethasone is also used as a direct chemotherapeutic agent in certain hematological malignancies, especially in the treatment of multiple myeloma, in which dexamethasone is given alone or in combination with other chemotherapeutic drugs, including most commonly with thalidomide (thal-dex), lenalidomide, bortezomib (Velcade; Vel-dex)[21] , or a combination of Adriamycin (doxorubicin) and vincristine (VAD).

Endocrine

Dexamethasone is the treatment for the very rare disorder of glucocorticoid resistance.[22] [23]

In adrenal insufficiency and Addison's disease, dexamethasone is prescribed when the person doesn't respond well to prednisone or methylprednisolone.

Obstetrics

Dexamethasone may be given to women at risk of delivering prematurely in order to promote maturation of the fetus' lungs. This has been associated with low birth weight, although not with increased rates of neonatal death.[24]

High altitude illnesses

Dexamethasone is used in the treatment of high altitude cerebral edema as well as pulmonary edema. It is commonly carried on mountain climbing expeditions to help climbers deal with altitude sickness. British mountain climber Peter Kinloch was provided with a shot of dexamethasone shortly before his death, after summiting Mount Everest.[25] [26]

Off-label use

Congenital adrenal hyperplasia

Dexamethasone has been used as an off-label pre-natal treatment for the symptoms of congenital adrenal hyperplasia (CAH) in female fetuses. CAH causes a variety of physical abnormalities, notably ambiguous genitalia in girls. Early pre-natal CAH treatment has been shown to reduce some CAH symptoms, but it does not treat the underlying congenital disorder.

A 2007 Swedish clinical trial found that treatment may cause cognitive and behavioural defects, but the small number of test subjects means the study cannot be considered definitive. Administration of pre-natal dexamethasone has been the subject of controversy over issues of informed consent and because treatment must predate a clinical diagnosis of CAH in the female fetus.[27]

A medical consensus in 2010 by the Endocrine Society and affiliated organizations indicated that prenatal dexamethasone for CAH should be regarded as experimental and should only be used in Institutional Review Board-approved controlled clinical trials at centers large enough to collect meaningful data.[28]

Abuses

Dexamethasone has also been used in the hope of enhancing sports performance.[29]

Long term use of dexamethasone under the brand name Oradexon is widespread among prostitutes in Bangladesh in spite of the dangers, because it helps them develop fat easily, an attractive feature in this poor country.[30] [31]

Diagnostic use

Dexamethasone is also used in a diagnostic context, namely in its property to suppress the natural pituitary-adrenal axis. Patients presenting with clinical signs of glucocorticoid excess (Cushing's syndrome) are generally diagnosed by a 24-hour urine collection for cortisol or by a dexamethasone suppression test. During the latter, the response of

the body to a high dose of glucocorticoids is monitored. Various forms are performed. In the most common form, a patient takes a nighttime dose of either 1 or 4 mg of dexamethasone, and the serum cortisol levels are measured in the morning. If the levels are relatively high (over 5 µg/dL or 150 nmol/L), then the test is positive and the patient has an autonomous source of either cortisol or ACTH, indicating Cushing's syndrome where the tumor does not have a feedback mechanism. If ACTH levels are lowered by at least 50%, this would indicate Cushing's Disease, since the pituitary adenoma has a feedback mechanism that has been reset to a higher level of cortisol. Longer versions rely on urine collections on oral dexamethasone over various days.

Veterinary use

Combined with marbofloxacin and clotrimazole, dexamethasone is available under the name *Aurizon* , CAS number 115550-35-1, and used to treat difficult ear infections, especially in dogs. It can also be combined with Trichlormethiazide to treat horses with swelling of distal limbs and general bruising.[32]

Contraindications

Some of these contraindications are relative:

- Existing gastrointestinal ulceration
- Cushing's syndrome
- Severe forms of heart insufficiency
- Severe hypertension
- Uncontrolled diabetes mellitus
- Systemic tuberculosis
- Severe systemic viral, bacterial, and fungal infections
- Preexisting wide angle glaucoma
- Osteoporosis

Side effects

If dexamethasone is given orally or by injection (parenteral) over a period of more than a few days, side-effects common to systemic glucocorticoids may occur. These may include:

- Stomach upset, increased sensitivity to stomach acid to the point of ulceration of esophagus, stomach, and duodenum
- Increased appetite leading to significant weight gain
- A latent diabetes mellitus often becomes manifest. Glucose intolerance is worsened in patients with preexisting diabetes.
- Immunsuppressant action, particularly if given together with other immunosuppressants such as cyclosporine. Bacterial, viral, and fungal disease may progress more easily and can become life-threatening. Fever as a warning symptom is often suppressed.
- Psychiatric disturbances, including personality changes, irritability, euphoria, mania
- Osteoporosis under long term treatment, pathologic fractures (e.g., hip)
- Muscle atrophy, negative protein balance (catabolism)
- Elevated liver enzymes, fatty liver degeneration (usually reversible)
- Cushingoid (syndrome resembling hyperactive adrenal cortex with increase in adiposity, hypertension, bone demineralization, etc.)
- Depression of the adrenal gland is usually seen, if more than 1.5 mg daily are given for more than three weeks to a month.

- Hypertension, fluid and sodium retention, edema, worsening of heart insufficiency (due to mineral corticoid activity)
- Dependence with withdrawal syndrome is frequently seen.
- Increased intraocular pressure, certain types of glaucoma, cataract (serious clouding of eye lenses)
- Dermatologic: Acne, allergic dermatitis, dry scaly skin, ecchymoses and petechiae, erythema, impaired wound-healing, increased sweating, rash, striae, suppression of reactions to skin tests, thin fragile skin, thinning scalp hair, urticaria.
- Allergic reactions (though infrequently): Anaphylactoid reaction, anaphylaxis, angioedema.

Other side-effects have been noted, and should cause concern if they are more than mild.

The short time treatment for allergic reaction, shock, and diagnostic purposes usually does not cause serious side effects.

Interactions

- NSAIDs and alcohol: increased risk of gastrointestinal ulceration
- Mineralocorticoids: increased risk of hypertension, edema and heart problems
- Oral antidiabetic drugs and insulin: antidiabetic therapy may have to be adjusted

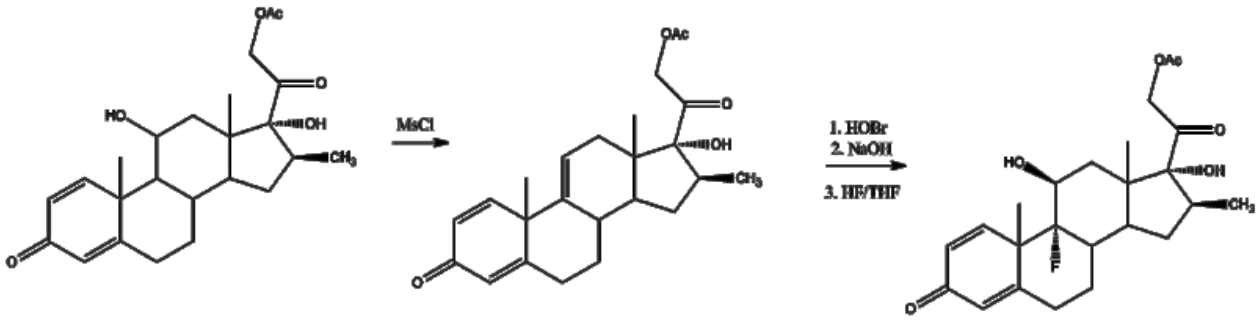
Other interactions (with certain antibiotics, estrogens, ephedrine, digoxin) are known.

Dosage

- Shock: 4 to 8 mg intravenously initially, repeat if necessary to a total dose of 24 mg.
- Autoimmune diseases and inflammations: longterm therapy with 0.5 to 1.5 mg oral per day. Avoid more than 1.5 mg daily, because serious side effects are more frequently encountered with higher doses.
- Adjuvant to or part of chemotherapy: individual schedule
- Diagnostic purposes: special schedule

Synthesis

To synthesise dexamethasone, 16β-methylprednisolone acetate is dehydrated to the 9,11 dehydro derivative. This is then reacted with a source of hypobromite such as basic N-bromosuccinimide to form the 9α-bromo-11β-hydrin derivative, which is then ring-closed to an epoxide. A ring opening reaction with hydrogen fluoride in tetrahydrofuran gives dexamethasone.[33] [34]



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External links

- Understanding Dexamethasone and Other Steroids (http://www.myeloma.org/main.jsp?source=link&source_link_id=2117&type=article&tab_id=13&menu_id=94&id=1749)
- U.S. National Library of Medicine: Drug Information Portal - Dexamethasone (http://druginfo.nlm.nih.gov/drugportal/dpdirect.jsp?name=Dexamethasone)

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