

Adrenocorticoids

- Synthesized in adrenal gland cortex.

HYPOTALAMUS

Cortikoliberin



PITUATRY

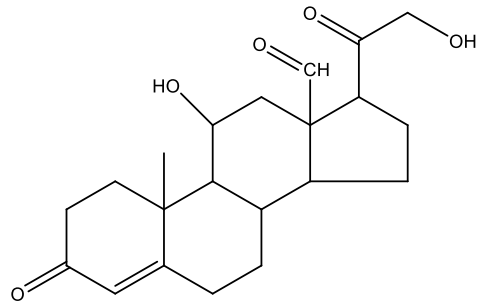
Corticotropine



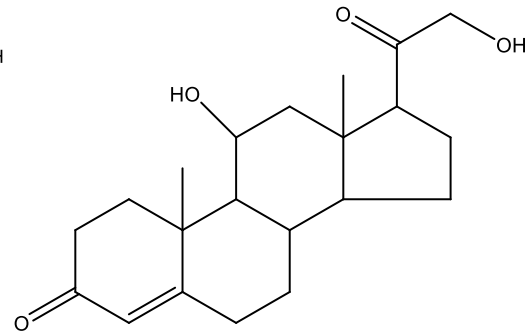
ADRENAL CORTEX

Adrenocortikoids

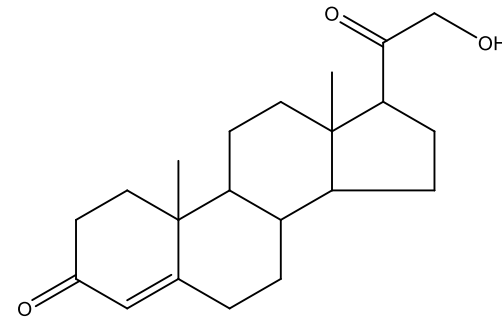
Biosynthesis is made from cholestole.



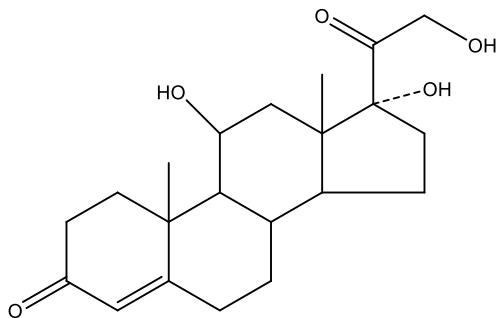
Aldosteron



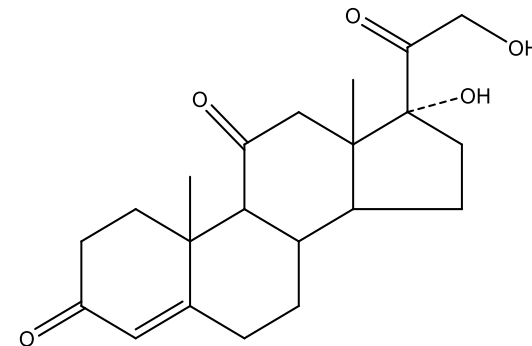
Corticosteron



Desoxycorticosteron



Hydrocortizone



Cortizone

Effects

Adrenocortikoids

Elektrolite and water balance → **mineralocorticoid effect**

Carbonhydrate, protein ve lipid metabolism → **glucocortikoid effect**

Blood muscle and sceleton system are effected → **glucocortikoid effect**

Mineralocorticoidal effects (dominant) aldosteron, corticosteron

→ mineralocorticoid

Glucocorticoidal effects (dominant) cortizone ve hydrocortizone

→ glucocorticoids

Mineralocorticoids → Na,Cl ve HCO₃ resorption

K excretion



Glucocorticoids ;

Glycogen stores in the liver, high doses of hyperglycemia and glycosuria make steroid diabetes, reduces sensitivity to insulin (irreversible effect),

Reduce protein synthesis in muscle and other tissues, increase lipid metabolism,

They reduce acid secretion in the stomach, but they may cause ulceration of the epithelium of the stomach and may cause ulcers (adrenocorticoid ulcer).

They act as anti-inflammatory by inhibiting the phospholipase A2 enzyme.

Uses

- Addison's disease (hypoadrenalism: adrenocorticoid hormone deficiency), treatment of diseases caused by insufficiency of congenital adrenal glands,
- Acute and chronic bronchial asthma,
- Acute drug reactions,
- In the treatment of allergic diseases such as contact dermatitis,
- They are also used directly and in combination with other drugs, some GI diseases, pulmonary diseases, blood table abnormalities, acute leukemia and lymphoma.
- Local dermatitis, eczema, allergic drug reactions, such as skin diseases, burning and various types of conjunctivitis, such as eye diseases, successful results.

There are also important places in the treatment of inflammatory connective tissue diseases such as rheumatoid arthritis, febrile arthritis, lupus erythematosus.

It is used to prevent acute exacerbations in multiple sclerosis (MS).

Side effects (acne, hair, back pain, menstrual disorders, etc.) similar to Cushing syndrome * are seen in high doses for a long time.

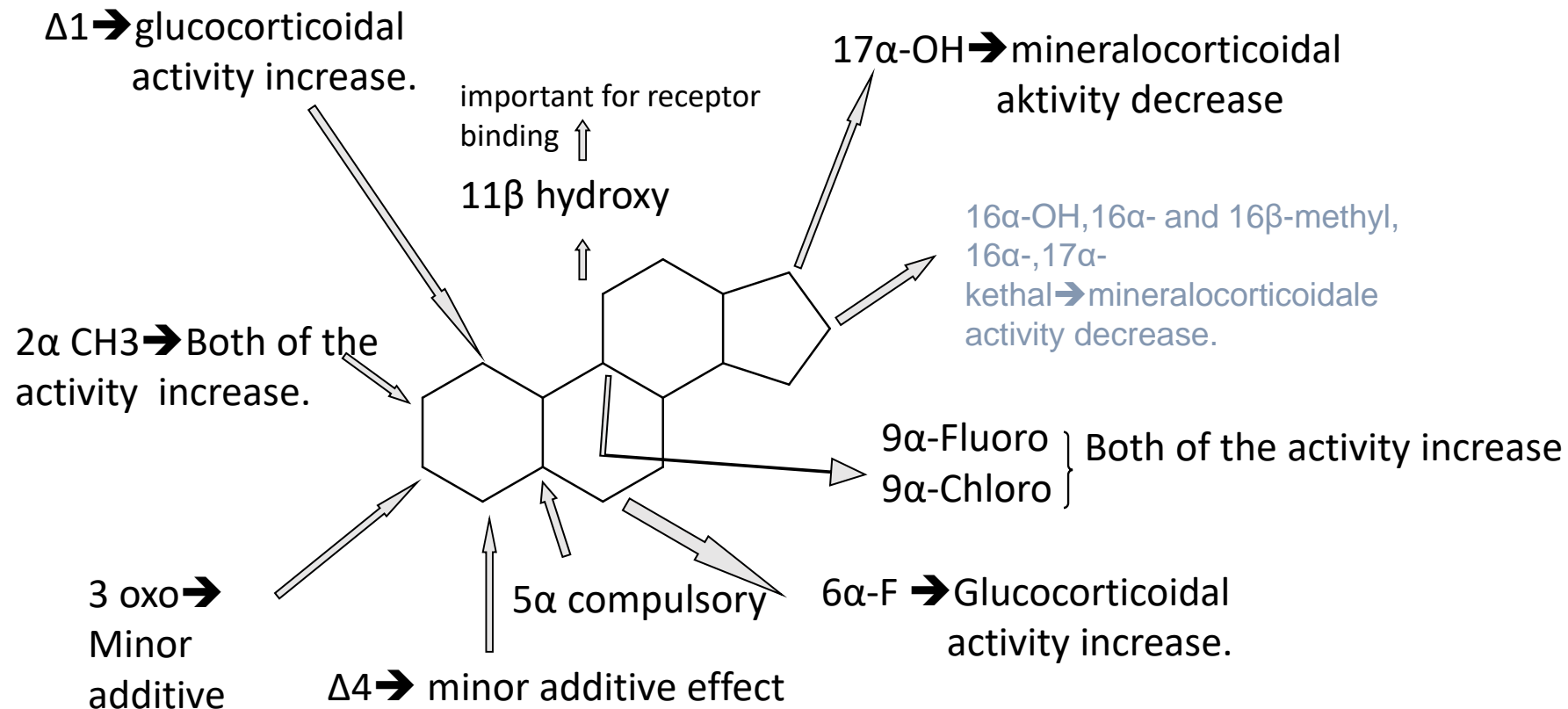
They usually do a slight blood pressure rise. Can make peptic ulcer and osteoporosis.

Quite often, they can be followed by depression and paranoid reactions.

Na-K equilibrium increases up to Na

* Cushing's Syndrome = hyperadrenalism

Structure Activity Relationship in Adrenocorticoids

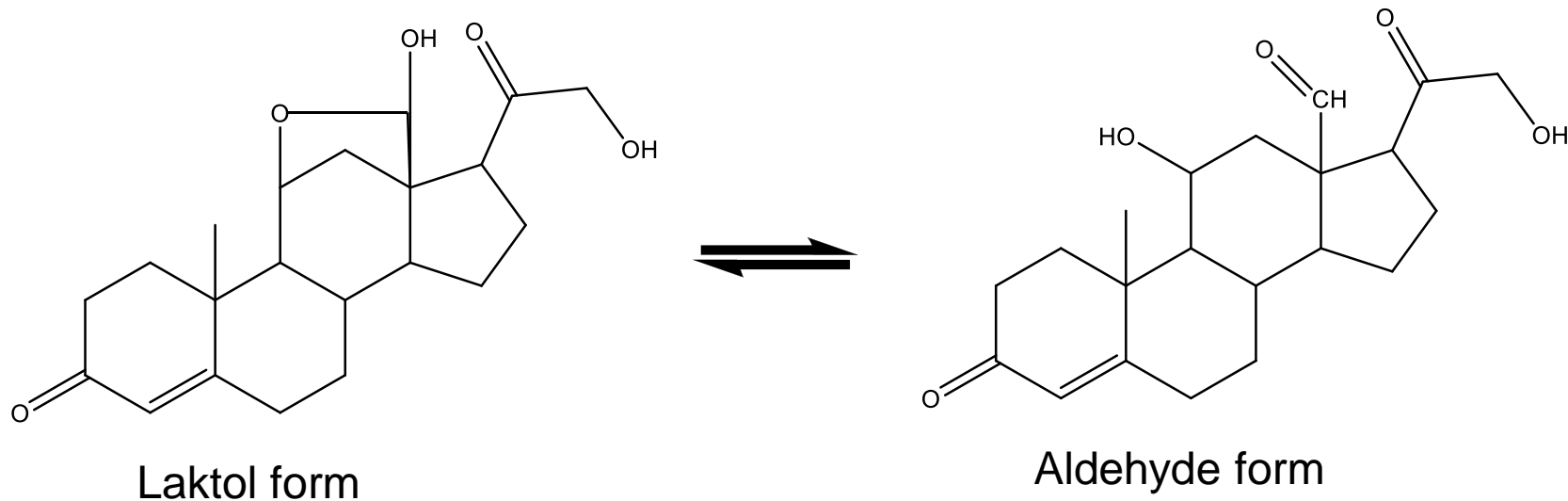


$\rightarrow 2\alpha \text{ CH}_3$ protect OH group on C-11 position against metabolic inactivation by sterically hindrance, drug's half-life is prolonged.

Adrenocorticoid Drugs

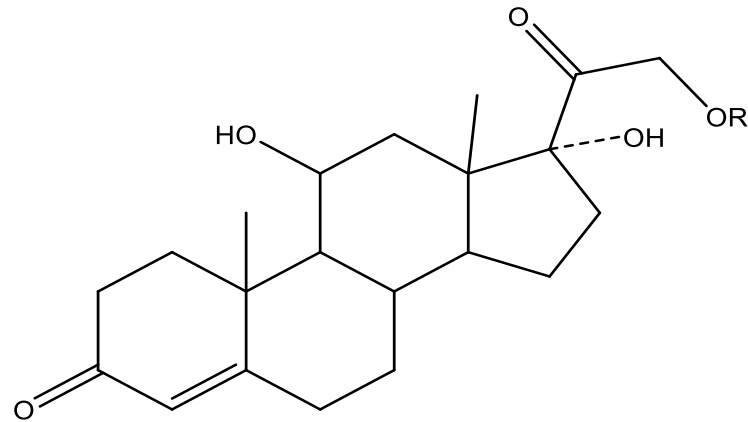
Aldosterone

Most active mineralocorticoid. It has no antiemflumatuar activity. Cause to sodium retantion and potassium excretion. Uses in Addison sickness. İ.V ve İ.M uses available.

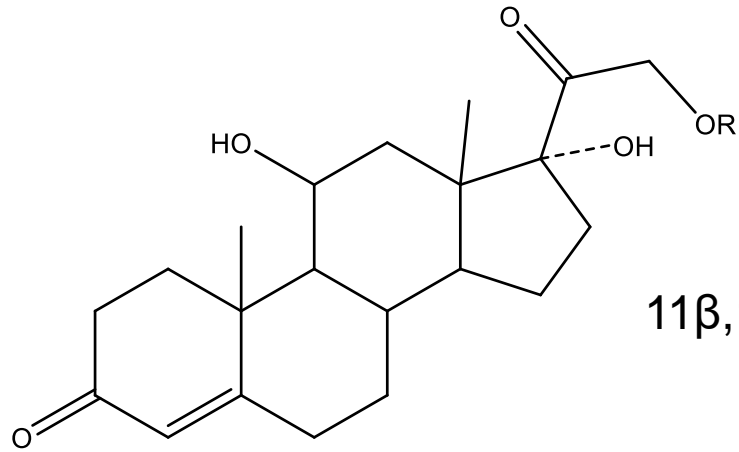


11 β ,21-dihydroxy-3,20-diokso pregn-4-en-18-al (11 18)laktol

Hydrocortizone



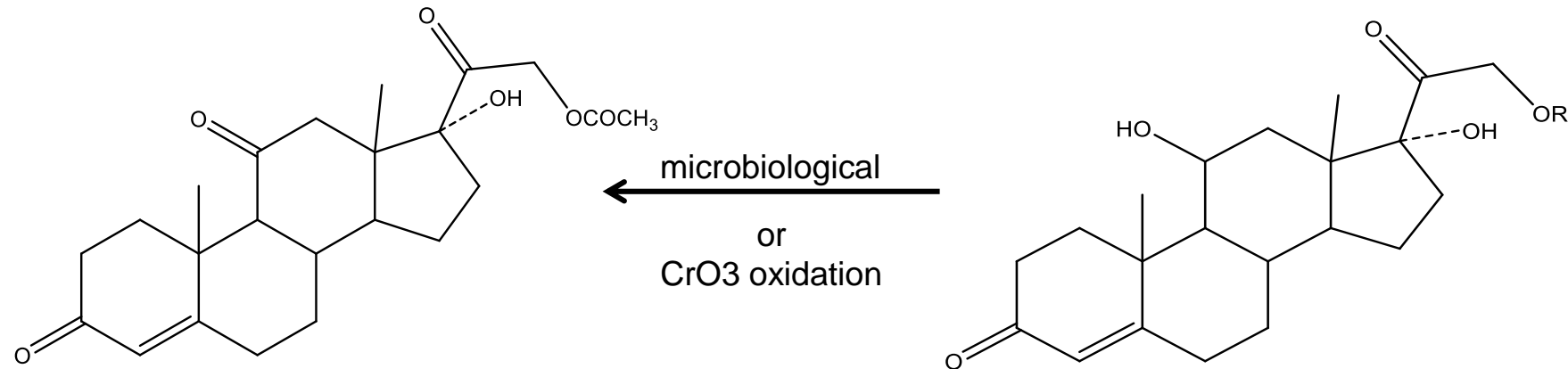
Used directly or in the form of esters. It is major glucocorticoid. There is also significant mineralocorticoid activity. Orally effective. It is used locally in Addison's disease and similar adrenal insufficiencies or in the treatment of oral or rectal, inflammatory or allergic skin diseases to provide a systemic **anti-inflammatory effect**.



11 β ,17 α ,21-trihydroxy pregn-4-en-3,20-dion

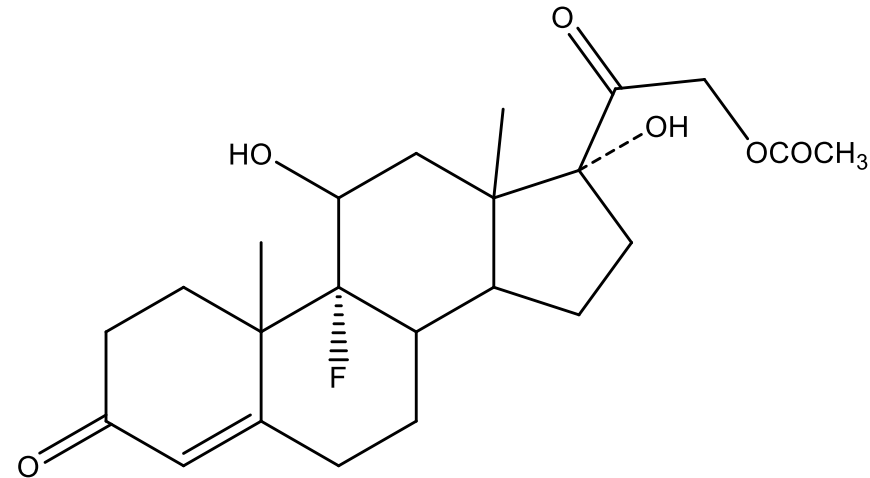
	R
Hydrocortizone acetate	-COCH ₃
Hydrocortizon hydrogen succinate	-COCH ₂ CH ₂ COOH
Hydrocortizon sodium succinate	-COCH ₂ CH ₂ COONa
Hydrocortizon sodium phosphate	

Cortizon acetate



Glucocorticoid and mineralocorticoid activity is 25 % lower than hydrocortisone.

Fludrocortizone acetate

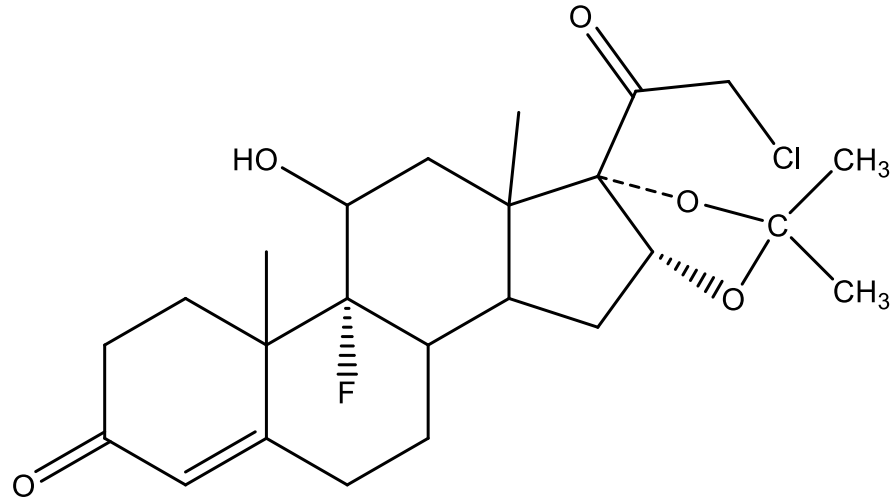


9 α -fluoro-11 β ,17 α , 21-trihydroxypregn-4-en-3,20-dion-21-acetate

Its antiinflammatory effect is 15 times and mineralocorticoid effect is 125 times higher than hydrocortisone.

Halsinonit

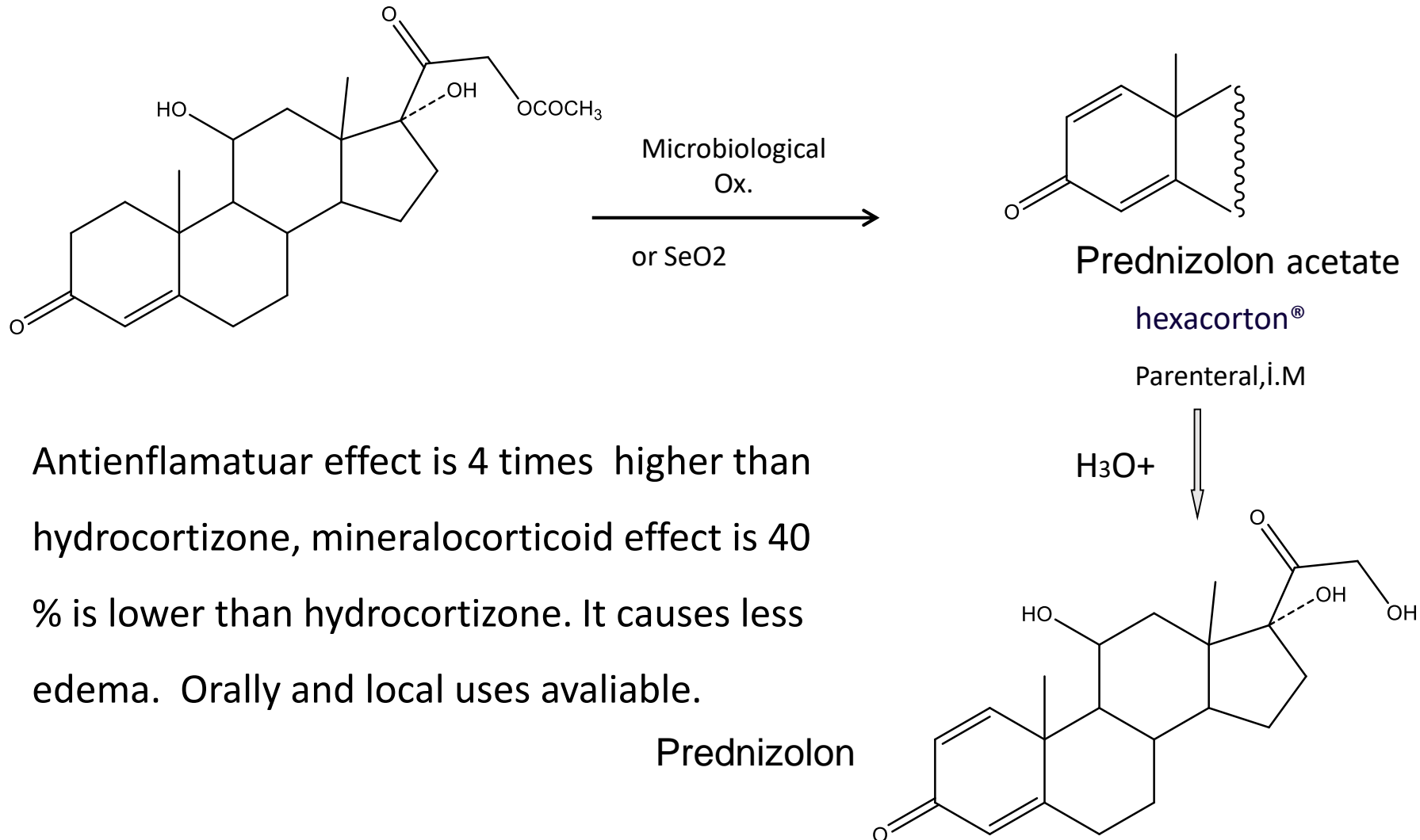
Betacorton[®], Volog[®]



9 α -fluoro-21-chloro-11 β ,16 α ,17 α -trihydroxypregn-4-en-3,20-dion
16,17-acetonide

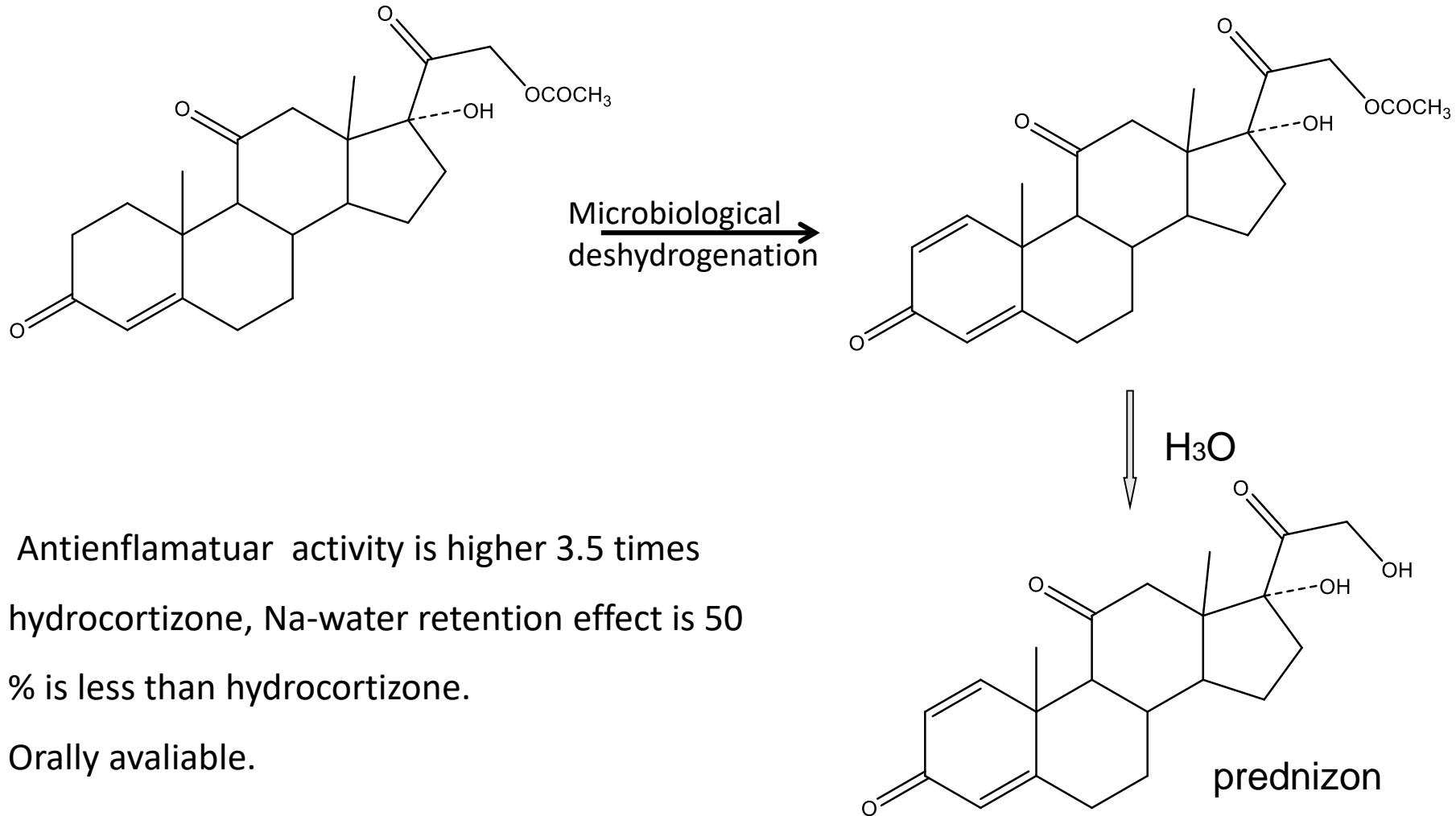
Used locally in inflammatory or allergic dermatoses

Prednizolon Deltacortil[®], Hexacorton[®], Prednol[®]



Antienflamatuar effect is 4 times higher than hydrocortizone, mineralocorticoid effect is 40 % is lower than hydrocortizone. It causes less edema. Orally and local uses available.

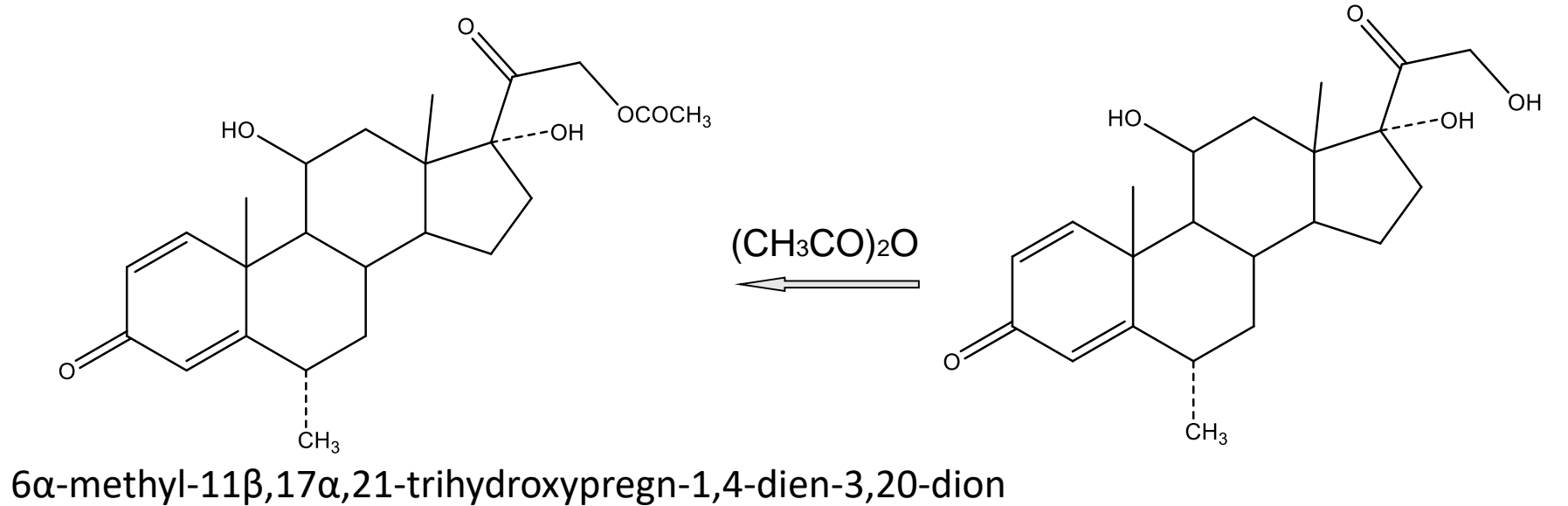
Prednison



Antienflamatuar activity is higher 3.5 times
hydrocortizone, Na-water retention effect is 50
% is less than hydrocortizone.
Orally available.

17 α ,21-dihydroxyipregn-1,4-dien-3,11,20-trion

Methylprednizolon Prednol®



6 α -methyl-11 β ,17 α ,21-trihydroxypregn-1,4-dien-3,20-dion

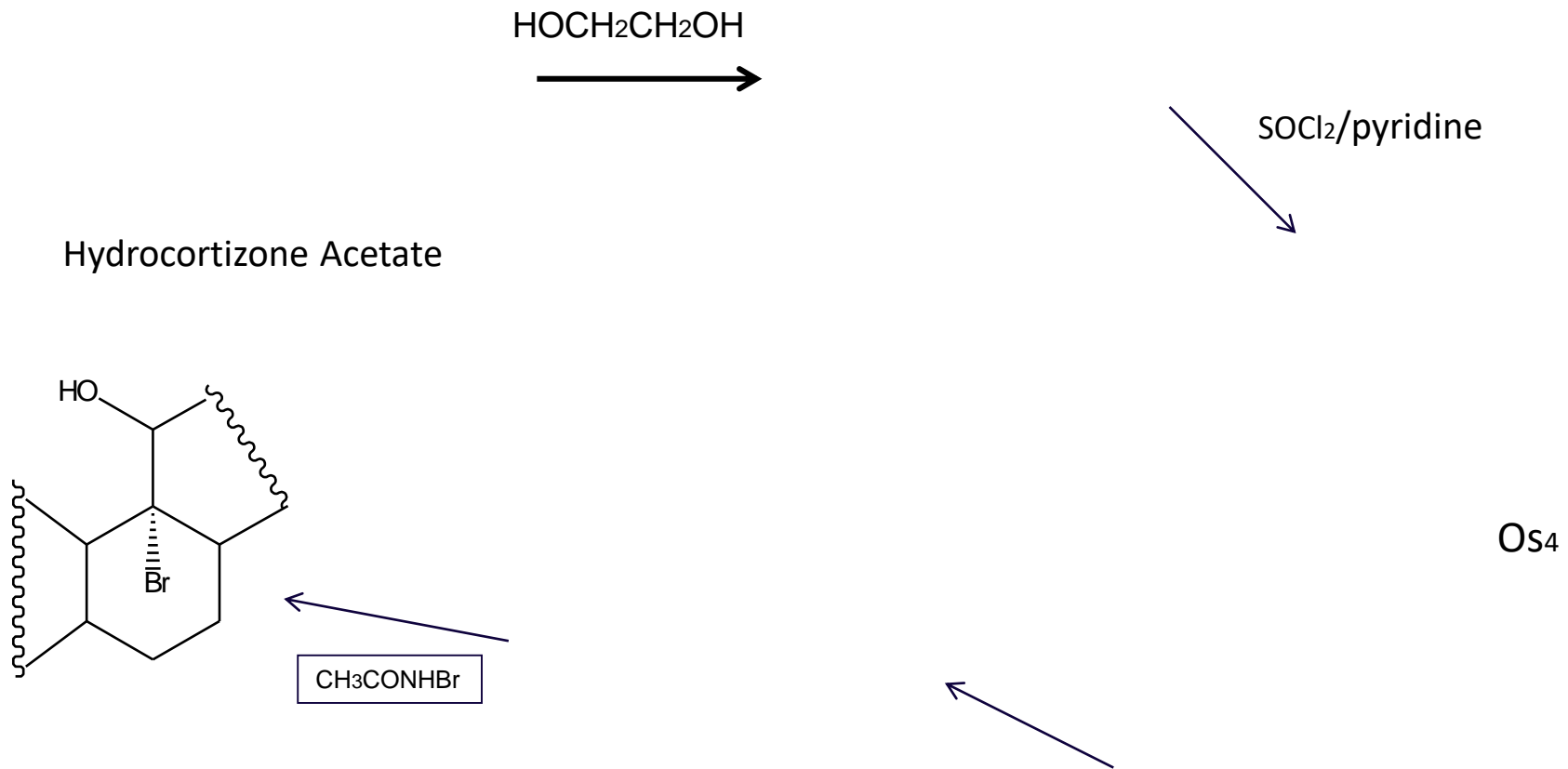
Methyl prednizolon : oral uses

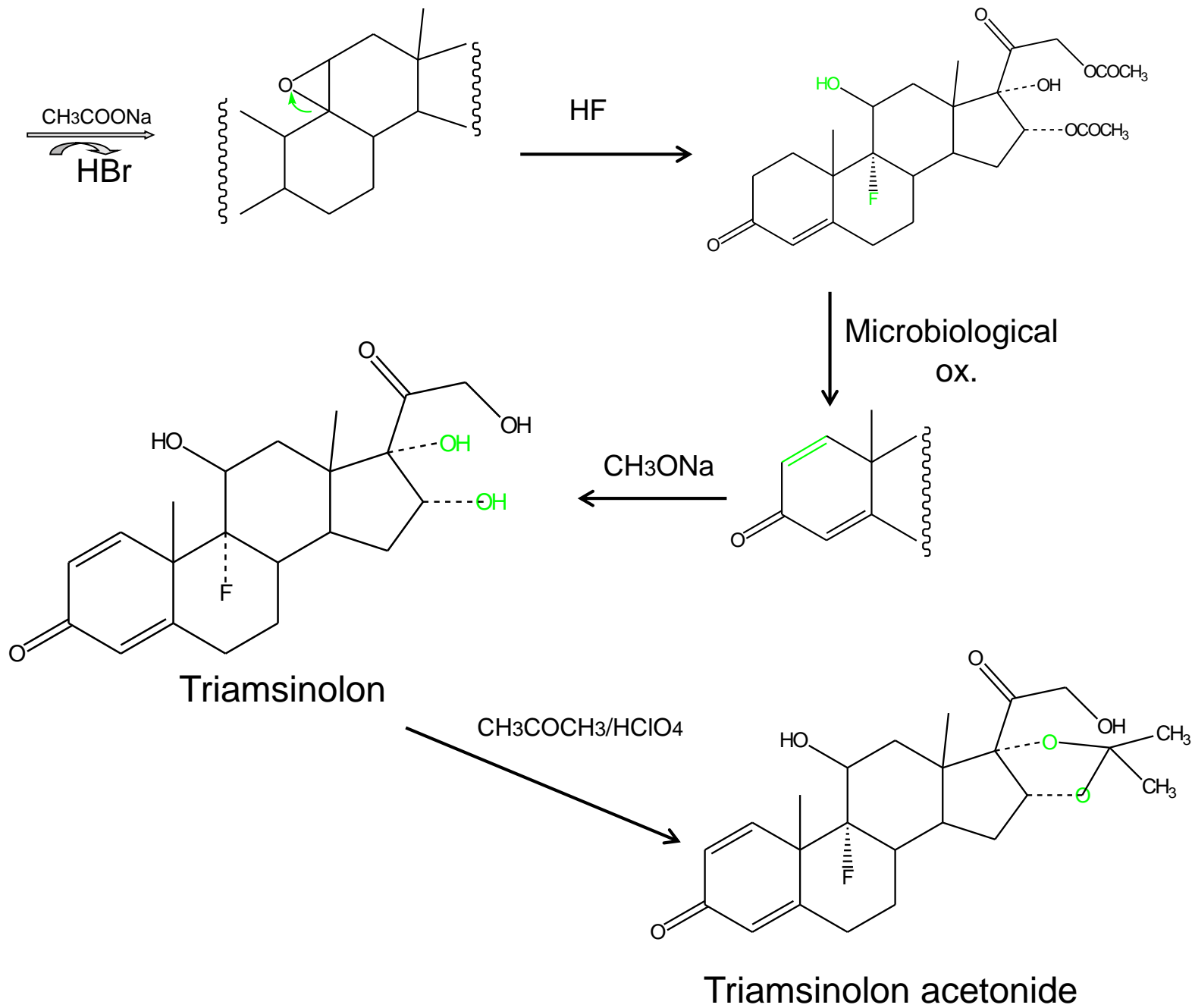
Methyl prednizolon acetate : parenteral
i.M, rectal, local

Antienflamatuar effect is higher than prednizolon, mineralocorticoid effect is less than prednizolon .

Triamnisolon

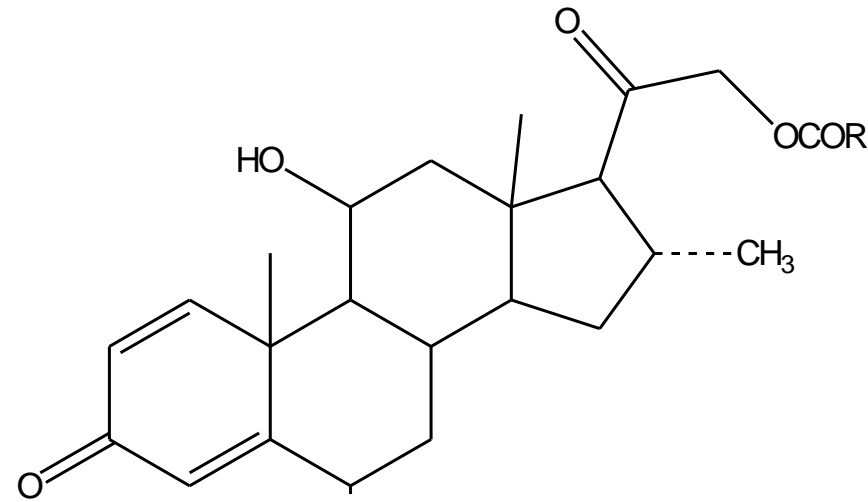
Triamsinolon acetone Kenacort®, Sinakort®





- Antienflammatuar effect → higher than prednison ve prednizolon, equal to methylprednizolon.
- Mineralocorticoide activity almost totally disapperaed.
Orally uses avaiable.
- Triamsinolon acetonide → activity period is longer than triamsinolone. Parenteral, I.M, local → used in teeth paste, cream ve pomade .

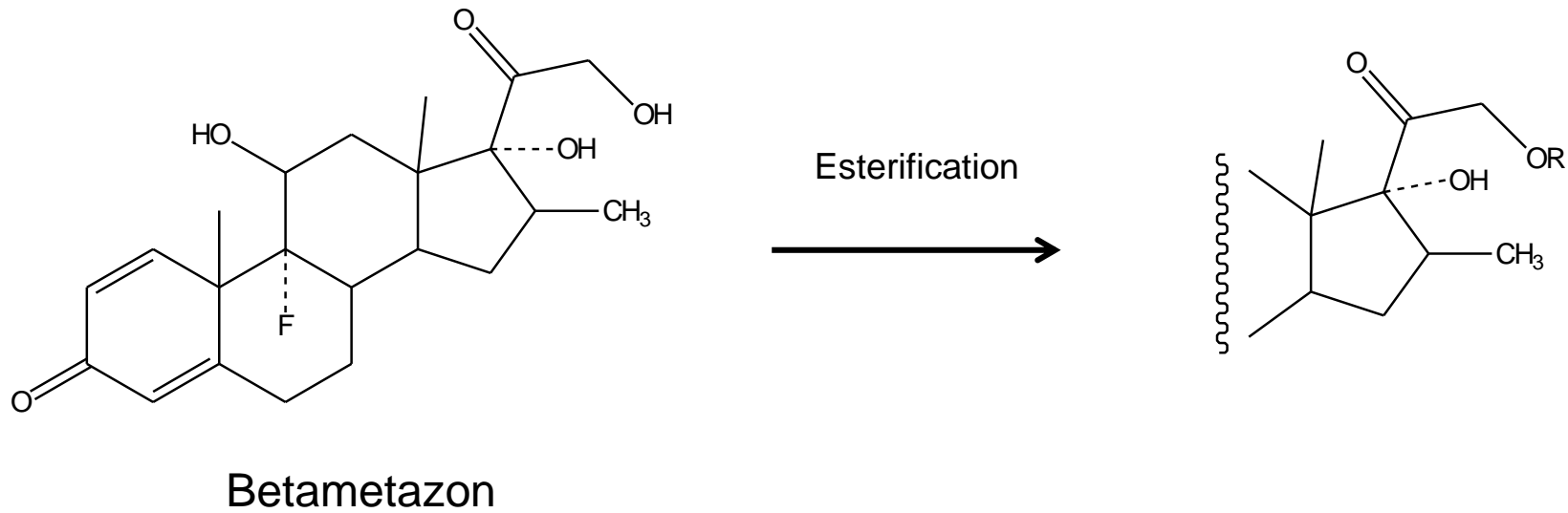
Flukortolon caproate (hexanoate) ve pivalate



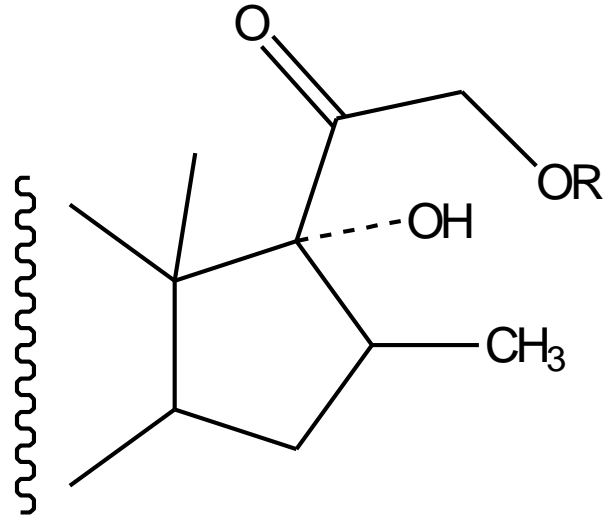
- For the treatment of inflammation and allergic dermatoses, it is used locally as a cream / pomade.

R = C₅H₁₁- Fluokortolon kaproat } Ultralan ®
(H₃C)₃C- Fluokortolon pivalat } Ultraproct ®

Betametazon Betnelan[®], Betnovate[®]

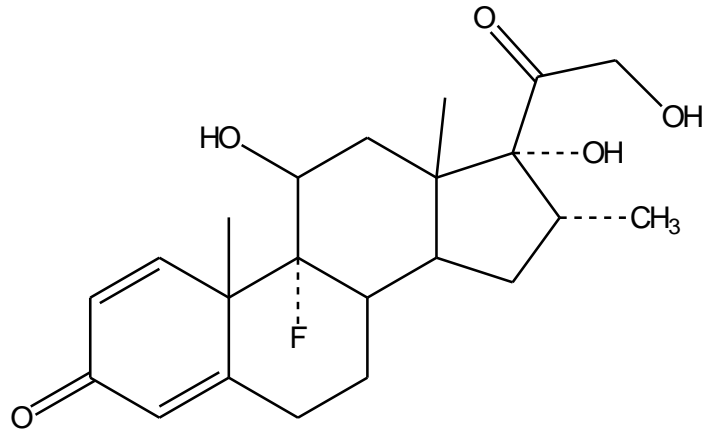


Most active antiinflammatory among the adrenocorticoids
Used directly or in the form of esters.



R	
-COCH₃	Betamethazone acetate
-CO(CH₂)₃CH₃	Betamethazone valerate
-PO₃Na₂	Betamethazone sodium phosphate

Dexamethazone Dekort[®], Deksalon[®], Deksamet[®]



As systematic antienflamatuar → tablet, local

9 α -fluoro-11 β ,17 α ,21-trihydroxy-16 α -methylpregn-1,4-dien-3,20-dion

Dexamethazone sodium phosphate → Cebedex[®], Deksamet[®]

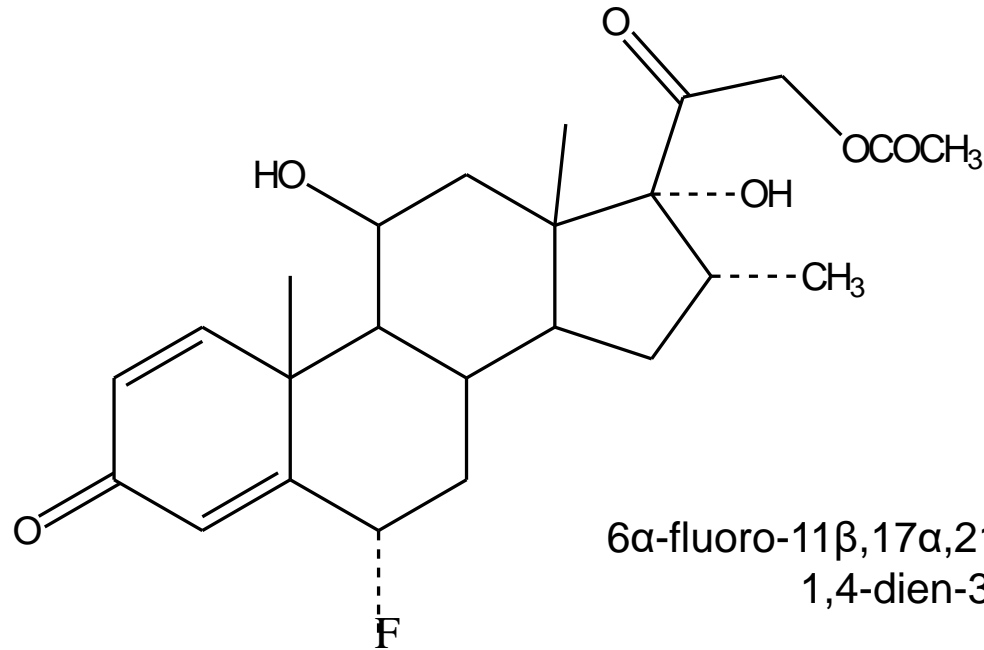
→ parenteral and local

IV,IM

Intraarticuler

- Dexamethasone sodium phosphate and dexamethasone acetate are antiinflammatory and immunosuppressive compounds.
- Mineralocorticoid activity is very weak. Since it is well penetrated to CNS, it is generally preferred in treatment of cerebral edema.
- Stronger than 20-30 times than hydrocortisone, 5 -7 times than prednisone.

Paramethazone acetate Depo-Dilar®

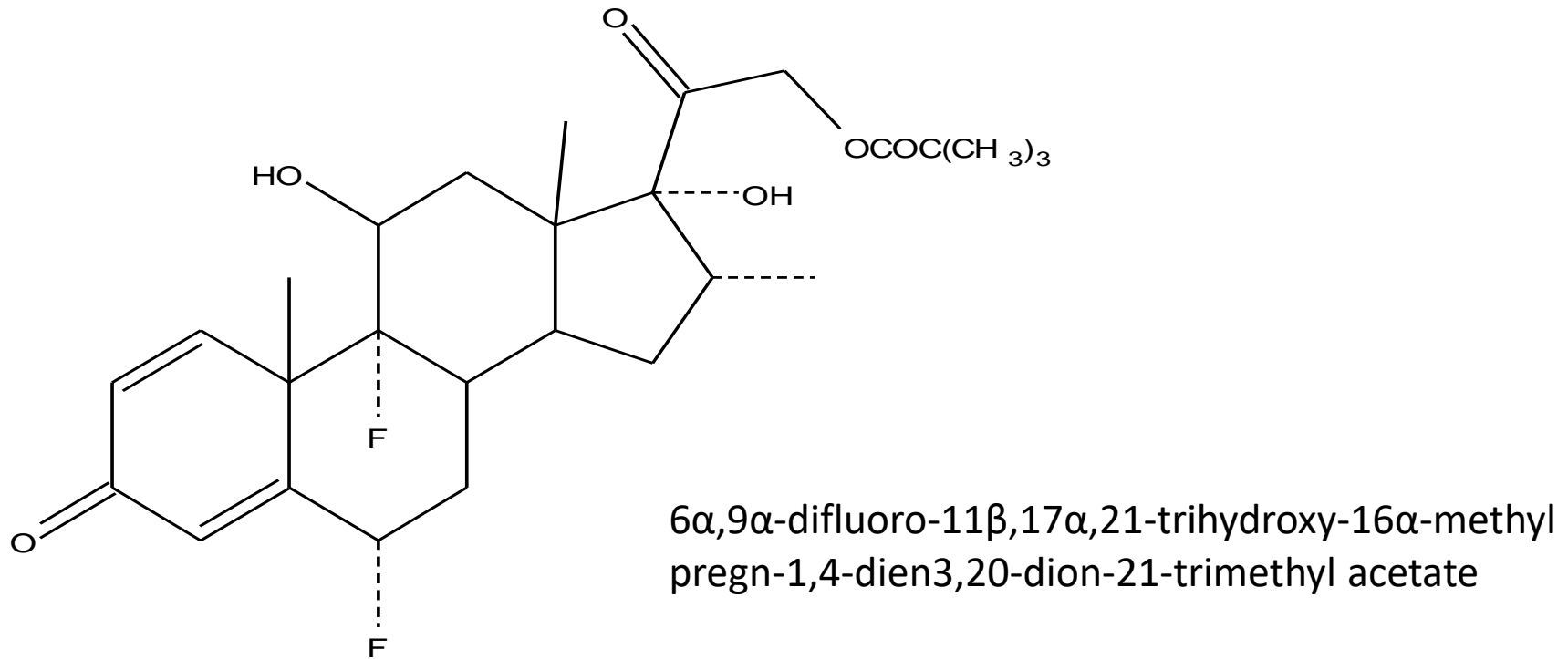


6α-fluoro-11β,17α,21-trihydroxy-16α-methylpregn-1,4-dien-3,20-dione 21 acetate

It is 10 times more active than hydrocortisone and 2.5 times more than prednisolone.

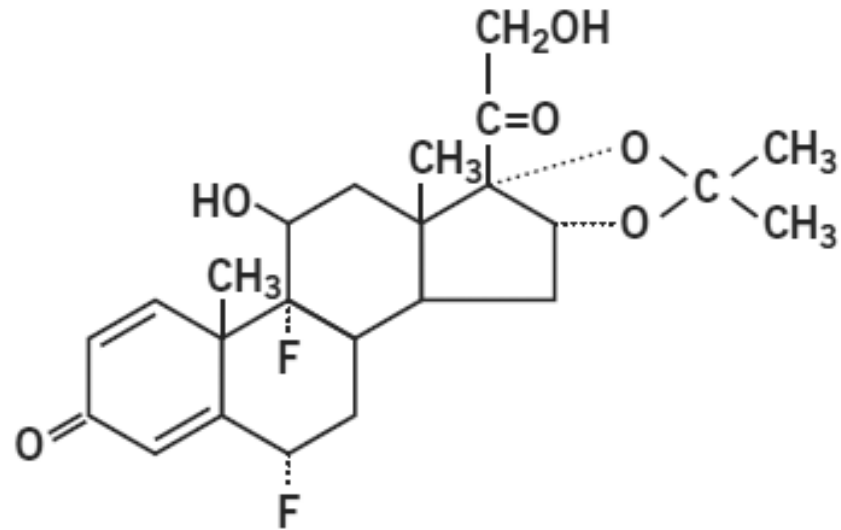
It is used as antiinflammatory and antiallergic oral and IM.

Flumethazon pivalate Locaselene[®], Locacortene[®]



Locally used in the treatment of inflammatory skin diseases

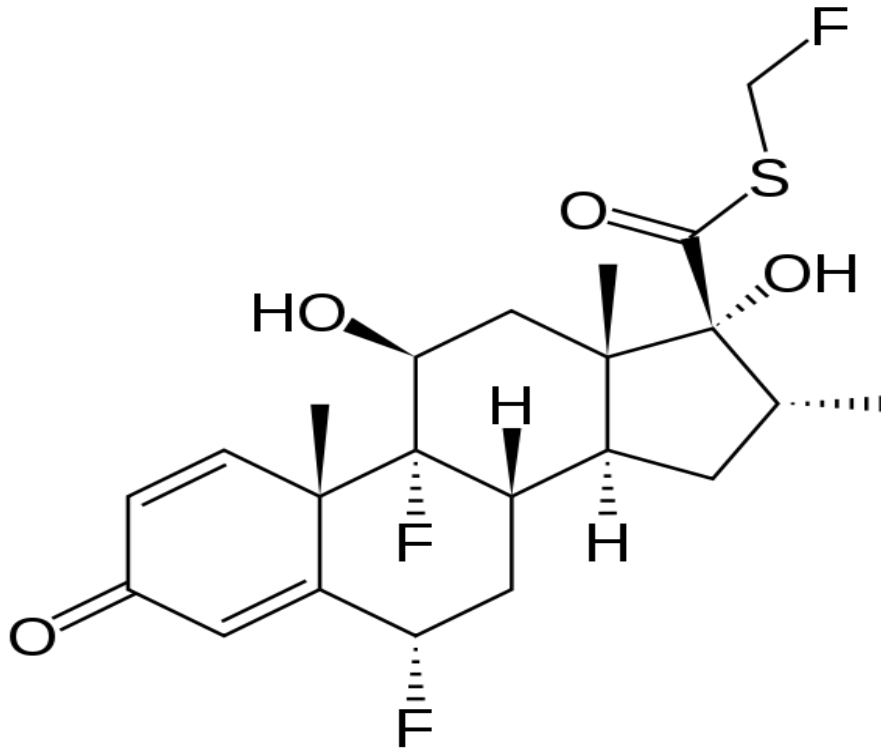
Flusinolon Myco-minalar®



6 α ,9 α -Difluoro-11 β ,16 α ,17 α ,21-tetrahydroxy-1,4-pregnadien-3,20-dion 16,17-asetonide

Locally used for the treatment of sensitive dermatitis and psoriasis.

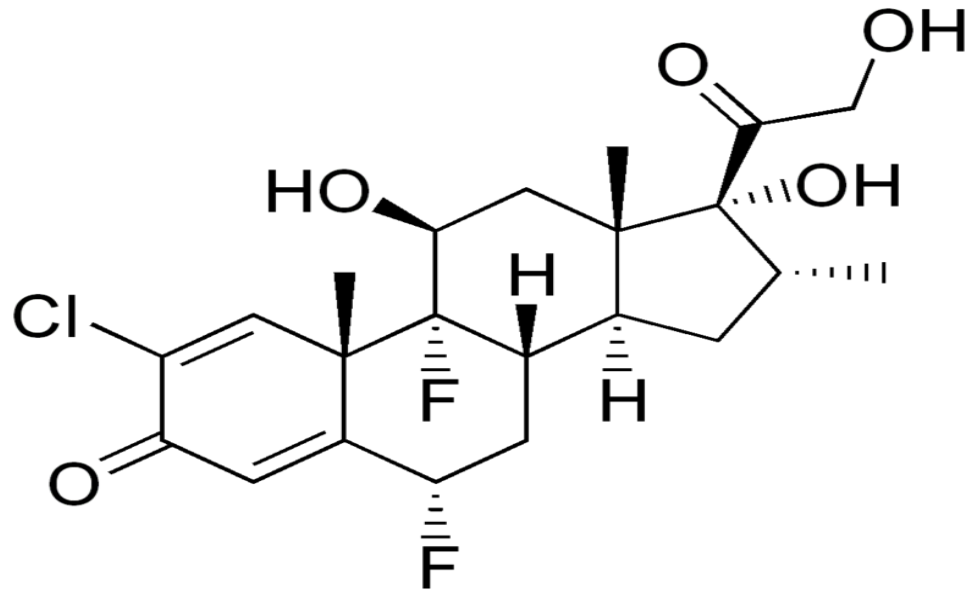
Flutikazon Cutivate[®], Brethal[®]



For dermatitis and psoriasis are used as locally for allergic rhinitis and asthma as nasal inhalear.

S-Fluorometil-6 α ,9 α -difluoro-11 β ,17 α -dihydroxy-16 α -methyl-3-oxo- androsta-1,4-dien-17 β -karbothioate

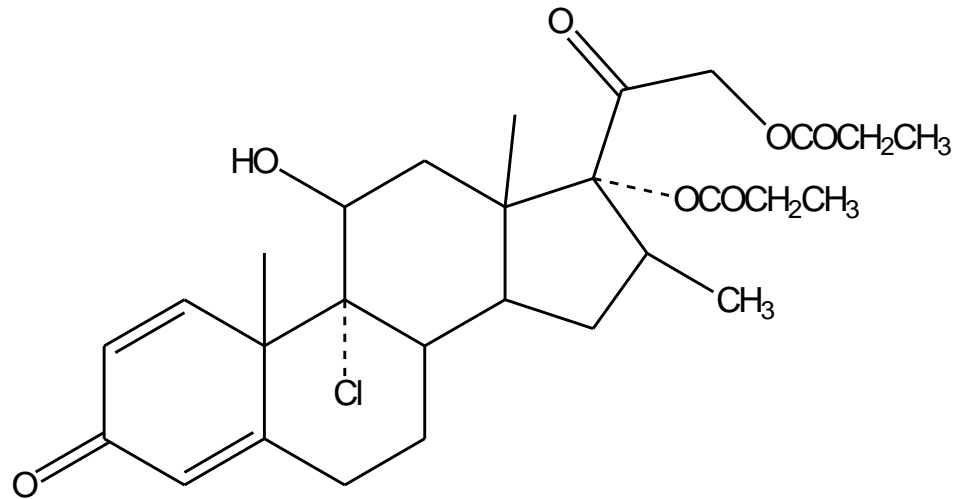
Halometazon Sicorten®



Used locally in skin diseases.

2-Chloro-6 α ,9 α -difluoro-11 β ,17 α ,21-trihydroxy-16 α -methylpregn-1,4-dien-3,20-dione

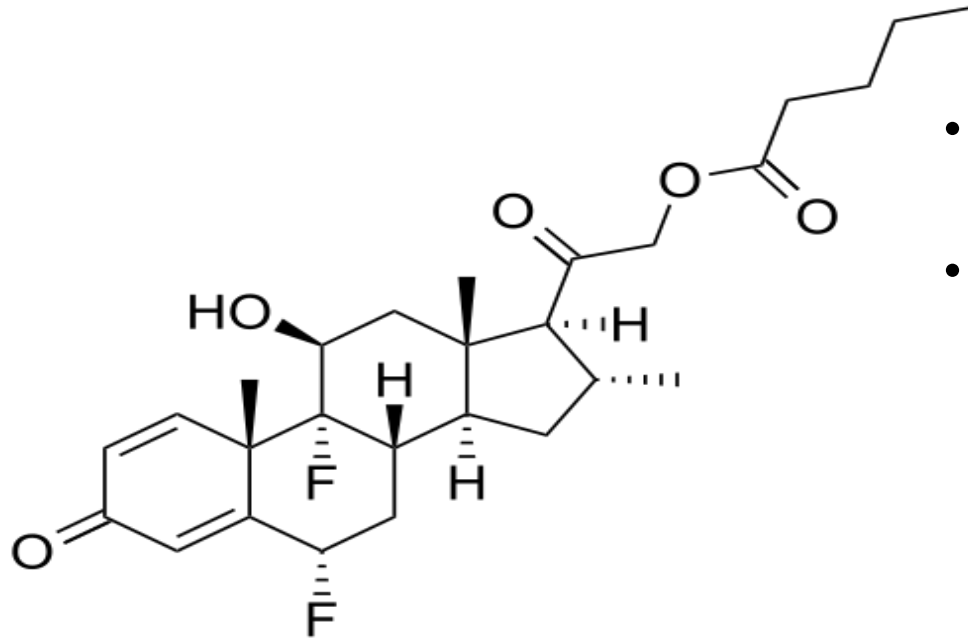
Beklometazon dipropiyonate Beclaforte[®], Beklazon[®], Beklomet[®]



9 α -Chloro-11 β ,17 α ,21-trihydroxy-16 β -methylpregn-1,4-dien-3,20-dion-17,21-dipropiyonate.

- Chlorinated analogue of Bethametasone.
- For dermatose therapy as cream or pomade.
- For asthma therapy.

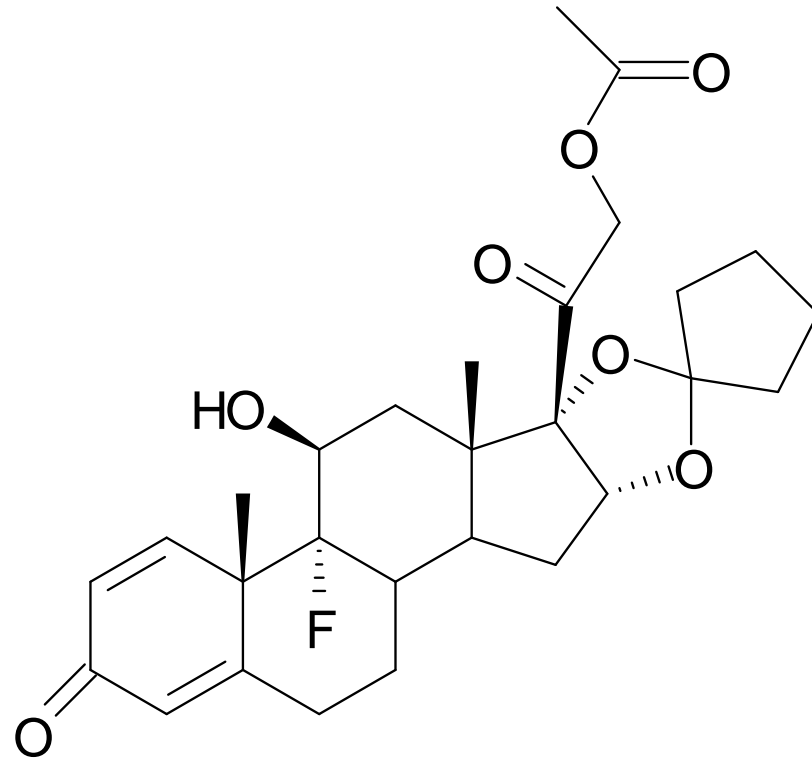
Diflukortolon valerat Temetex[®] , Impetex[®]



- Antienflamatuvar and antipruritic
- It is used locally in persistent skin diseases such as egzema

6 α , 9 α -Difluoro-11 β ,21-dihydroxy-16 α -methyl-3,20-dioxopregn-1,4-dien-21-pentanoate (valerate)

Amsinonid



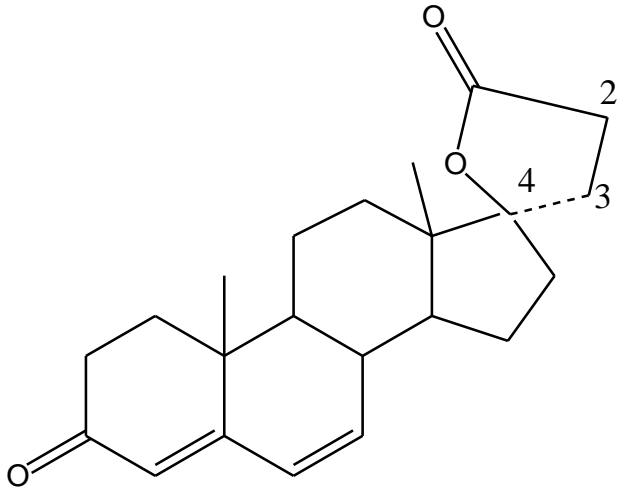
- One of the most strong local corticosteroids. Used as antiinflammatory and antipruritic.

- 16 α ,17 α -cyclopentilidendioxy-9 α -fluoro-11 β ,21-dihydroxy-pregn-1,4-dien-3,20-dion 21 acetate

Adrenocorticoid Antagonists

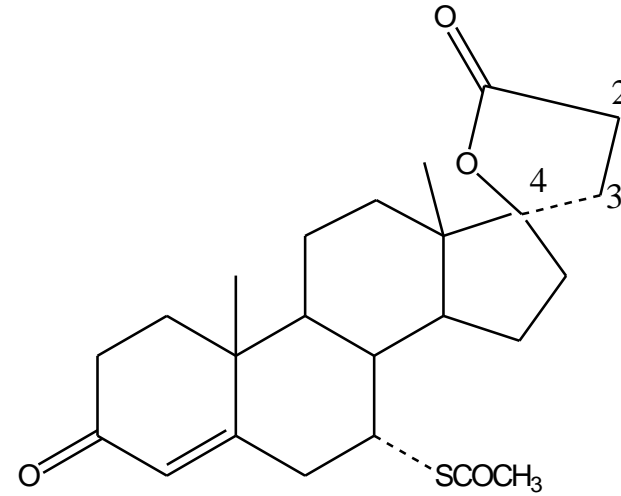
- Aldosterone - the ability to retain sodium ions – uses in congestive heart failure, nephrotic syndrome, cirrhosis of the liver, etc., leading to serious problems.

Kanrenone and spironolactone block aldosterone receptors in kidneys, so increases the excretion of sodium and chloride ions, some potassium and ammonium.



Kanrenon

17 β -hydroxy-3-oksopregna-4,6-dien-
21 carboxylic acid γ -lactone



spironolakton

17 β -hydroxy-7 α -mercaptopregna-
4-en-3-on-21-carboxylic acid γ lactone
-7-acetate

Glukocorticoid antagonist → MIFEPRISTON

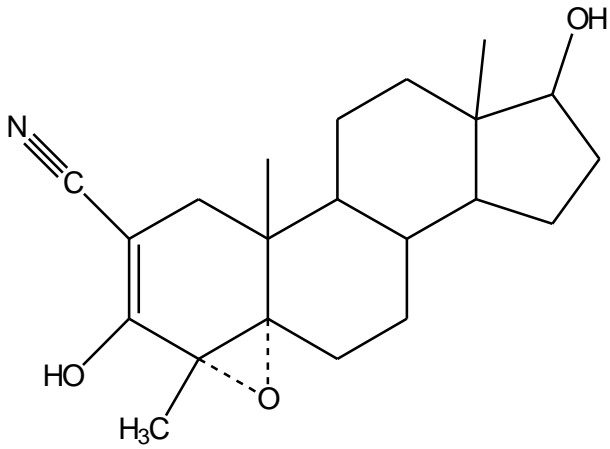
(PROGESTAGEN ANTAGONIST)



Antiglucocorticoidal
effect

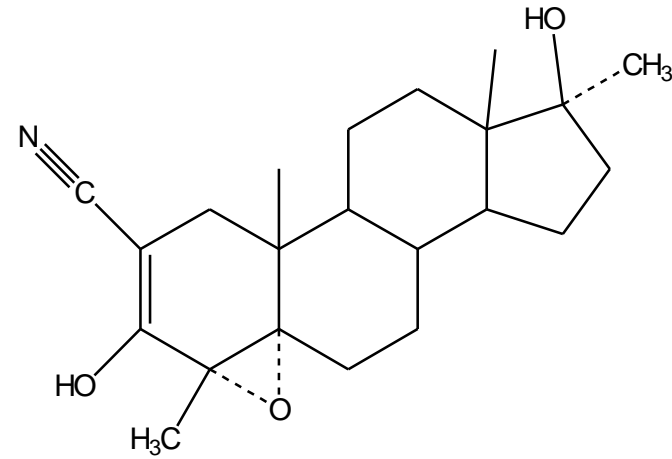
It inhibits mineralocorticoid and glucocorticoid synthesis

→ trilostan ve epostan → in hyperadrenalism therapy



Trilostan

4 α ,5 α -epoxy-4 β -methyl-
2-cyanoandrost-2-en-3,17 β -diol



Epostan

4 α ,5 α -epoxy-4 β ,17 α -dimethyl-
2-cyanoandrost-2-en-3,17 β -
diol

It is used as abortifacian in veterinary medicine. In order to suppress adrenocorticoid synthesis, for adrenal tumors are used orally in breast cancer and in cases of hyperadrenalism, etc.