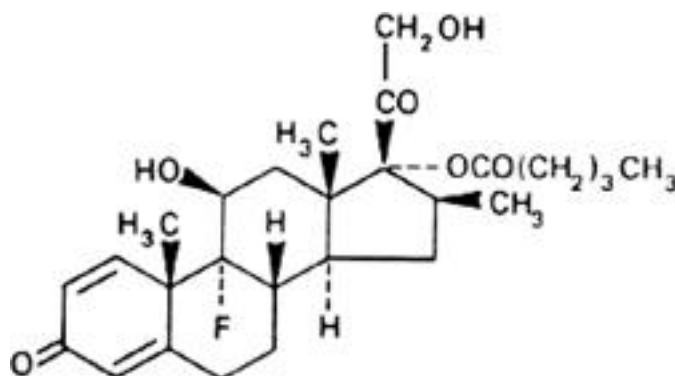


**Betamethasone valerate (Betamethasoni valeras)****Molecular formula.**  $C_{27}H_{37}FO_6$ **Relative molecular mass.** 476.6**Graphic formula.**

**Chemical name.** 9-Fluoro-11 $\beta$ ,17,21-trihydroxy-16 $\beta$ -methylpregna-1,4-diene-3,20-dione 17-valerate; 9-fluoro-11 $\beta$ ,21-dihydroxy-16 $\beta$ -methyl-17-[(1-oxopentyl)oxyl]pregna-1,4-diene-3,20-dione; CAS Reg. No. 2152-44-5.

**Description.** A white or creamy white powder; odourless.

**Solubility.** Practically insoluble in water; soluble in ethanol (~750 g/l)TS; freely soluble in acetone R.

**Category.** Antiinflammatory drug.

**Storage.** Betamethasone valerate should be kept in a tightly closed container, protected from light.

**Requirements**

**Definition.** Betamethasone valerate contains not less than 96.0% and not more than 104.0% of  $C_{27}H_{37}FO_6$ , calculated with reference to the dried substance.

**Identity tests**

• Either tests A and B or tests C, D and E may be applied.

A. Carry out the examination as described under [1.7 Spectrophotometry in the infrared region](#). The infrared absorption spectrum is concordant with the spectrum obtained from betamethasone valerate RS or with the *reference spectrum* of betamethasone valerate.

B. Dissolve 20 mg in 20 mL of ethanol (~750 g/l) TS and dilute 2 mL to 20 mL with the same solvent. To 2 mL of this solution placed in a stoppered test-tube add 10 mL of phenylhydrazine/sulfuric acid TS, mix, heat in a water-bath at 60 °C for 20 minutes, and cool immediately. The absorbance of a 1-cm layer at the maximum at about 423 nm is not more than 0.25.

C. See the test described below under "Related steroids". The principal spots obtained with solutions A and C correspond in position with that obtained with solution B. In addition, the principal spot obtained with solution A corresponds in appearance and intensity with that obtained with solution B.

D. Carry out the combustion as described under [2.4 Oxygen flask method](#), using 7 mg of the test substance and a mixture of 0.5 mL of sodium hydroxide (0.01 mol/l) VS and 20 mL of water as the absorbing liquid. When the process is complete, add 0.1 mL of a mixture of 0.1 mL of a freshly prepared sodium alizarinsulfonate (1 g/l) TS and 0.1 mL of zirconyl nitrate TS; the red colour of the solution changes to clear yellow.

E. Heat 0.05 g with 2.0 mL of potassium hydroxide/ethanol TS1 in a water-bath for 5 minutes. Cool, add 2.0 mL of sulfuric acid (~100 g/l) TS, and boil gently for 1 minute; a pleasant odour of ethyl valerate is perceptible.

**Specific optical rotation.** Use a 10 mg/mL solution in dioxan R;  $[\alpha]_D^{20} = +75^\circ$  to  $+81^\circ$ .

**Sulfated ash.** Weigh 0.1 g and ignite on a platinum dish; not more than 2.0 mg/g.

**Loss on drying.** Dry to constant weight at 105°C; it loses not more than 5.0 mg/g.

**Related steroids.** Carry out the test as described under [1.14.1 Chromatography, Thin-layer chromatography](#), using silica gel R1 as the coating substance and a mixture of 95 volumes of dichloroethane R, 5 volumes of methanol R, and 0.2 volumes of water

as the mobile phase. Apply separately to the plate 1 µl of each of 2 solutions in a mixture of 9 volumes of chloroform R and 1 volume of methanol R containing (A) 15 mg of the test substance per mL and (B) 15 mg of betamethasone valerate RS per mL; also apply to the plate 2 µl of a third solution (C) composed of a mixture of equal volumes of solutions A and B and 1 µl of a fourth solution (D) containing 0.15 mg of the test substance per mL in the same solvent mixture used for solutions A and B. After removing the plate from the chromatographic chamber, allow it to dry in air until the solvents have evaporated. Then heat it at 105 °C for 10 minutes, allow it to cool, spray it with blue tetrazolium/sodium hydroxide TS, and examine the chromatogram in daylight. Any spot obtained with solution A, other than the principal spot, is not more intense than that obtained with solution D.

### Assay

- The solutions must be protected from light throughout the assay.

Dissolve about 20 mg, accurately weighed, in sufficient aldehyde-free ethanol (~750 g/l) TS to produce 100 mL. Dilute 20 mL of this solution with sufficient aldehyde-free ethanol (~750 g/l) TS to produce 100 mL. Transfer 10.0 mL of the diluted solution to a 25-mL volumetric flask, add 2.0 mL of blue tetrazolium/ethanol TS, and displace the air in the flask with oxygen-free nitrogen R. Immediately add 2.0 mL of tetramethylammonium hydroxide/ethanol TS and again displace the air with oxygen-free nitrogen R. Stopper the flask, mix the contents by gentle swirling, and allow to stand for 1 hour in a water-bath at 30 °C. Cool rapidly, add sufficient aldehyde-free ethanol (~750 g/l) TS to produce 25 mL, and mix. Measure the absorbance of a 1-cm layer at the maximum at about 525 nm against a solvent cell containing a solution prepared by treating 10 mL of aldehyde-free ethanol (~750 g/l) TS in a similar manner. Calculate the amount of  $C_{27}H_{37}FO_6$  in the substance being tested by comparison with betamethasone valerate RS, similarly and concurrently examined.