FLUNIXIN MEGLUMINE FOR VETERINARY USE

Flunixin megluminum ad usum veterinarium

C₂₁H₂₈F₃N₃O₇

M, 491.5

DEFINITION


Content: 99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: freely soluble in water and in methanol, practically insoluble in acetone.

IDENTIFICATION

A. Specific optical rotation (2.2.7): –9.0 to –12.0 (dried substance), determined on solution S (see Tests).

B. Infrared absorption spectrophotometry (2.2.24).

Comparison: flunixin meglumine CRS.

TESTS

Solution S. Dissolve 2.50 g in carbon dioxide-free water R and dilute to 50.0 ml with the same solvent.

Appearance of solution. Solution S is clear (2.2.1) and not more intensely coloured than reference solution Y7 (2.2.2, Method II).

pH (2.2.3): 7.0 to 9.0 for solution S.

Related substances. Liquid chromatography (2.2.29).

Test solution. Dissolve 50.0 mg of the substance to be examined in the mobile phase and dilute to 10.0 ml with the mobile phase.

Reference solution (a). Dissolve 5.0 mg of flunixin impurity B CRS in 1.0 ml of the test solution and dilute to 50.0 ml with the mobile phase.

Reference solution (b). Dissolve 5.0 mg of 2-chloronicotinic acid R (impurity A) in the mobile phase and dilute to 50.0 ml with the mobile phase. To 2.0 ml of this solution add 2.0 ml of reference solution (a) and dilute to 20.0 ml with the mobile phase.

Reference solution (c). Dissolve 50 mg of flunixin impurity C CRS in the mobile phase and dilute to 100 ml with the mobile phase.

Column:
- size: l = 0.125 m, Ø = 4.0 mm,
- stationary phase: octadecylsilyl silica gel for chromatography R (5 µm).

Flow rate: 1.0 ml/min.

Detection: spectrophotometer at 254 nm.

Injection: 10 µl.

Run time: 5 times the retention time of flunixin.

Relative retention with reference to flunixin (retention time = about 3.1 min): impurity A = about 0.4; impurity C = about 0.6; impurity B = about 0.7; impurity D = about 4.2.

System suitability: reference solution (a):
- resolution: minimum 3.5 between the peaks due to impurity B and flunixin.

Limits:
- correction factor: for the calculation of content, multiply the peak area of impurity C by 1.9.
- impurity A: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.2 per cent).
- impurity B: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.2 per cent).
- impurities C, D: for each impurity, not more than the area of the peak due to flunixin in the chromatogram obtained with reference solution (b) (0.2 per cent),
- any other impurity: for each impurity, not more than the area of the peak due to flunixin in the chromatogram obtained with reference solution (b) (0.5 per cent),
- disregard limit: 0.25 times the area of the peak due to flunixin in the chromatogram obtained with reference solution (b) (0.05 per cent).

ASSAY

Dissolve 0.175 g in 50 ml of anhydrous acetic acid R. Titrate with 0.1 M perchloric acid, determining the end-point potentiometrically (2.2.20).

1 ml of 0.1 M perchloric acid is equivalent to 24.57 mg of C₂₁H₂₈F₃N₃O₇.

IMPURITIES

Specified impurities: A, B, C, D.

A. R = H: 2-chloropyridine-3-carboxylic acid,

C. R = C₆H₅: ethyl 2-chloropyridine-3-carboxylate,

B. 2-methyl-3-(trifluoromethyl)aniline,
**EUROPEAN PHARMACOPOEIA 6.0**

**Fluocinolone acetonide**

**D. ethyl 2-[2-methyl-3-(trifluoromethyl)phenyl]amino]pyridine-3-carboxylate.**

01/2008:0494 corrected 6.0

**FLUOCINOLONE ACETONIDE**

**Fluocinoloni acetonidum**

C\textsubscript{24}H\textsubscript{30}F\textsubscript{2}O\textsubscript{6}  
M \textsubscript{r} 452.5  
[67-73-2]

**DEFINITION**

α,9-Difluoro-11β,21-dihydroxy-16α,17-(1-methylethylidene-dioxy)pregna-1,4-diene-3,20-dione.

**Content**: 97.0 per cent to 103.0 per cent (dried substance).

**CHARACTERS**

**Appearance**: white or almost white, crystalline powder.

**Solubility**: practically insoluble in water, soluble in acetone and in ethanol.

It shows polymorphism (5.9).

**IDENTIFICATION**

A. Infrared absorption spectrophotometry (2.2.24).

**Comparison**: fluocinolone acetonide CRS.

If the spectra obtained in the solid state show differences, dissolve the substance to be examined and the reference substance separately in ethanol \( R \) and evaporate to dryness and record new spectra using the residues.

B. Examine the chromatograms obtained in the test for related substances.

**Results**: the principal peak in the chromatogram obtained with the reference solution (b) is similar in retention time to the peak due to fluocinolone acetonide CRS in the chromatogram obtained with the reference solution (a).

**TESTS**

**Specific optical rotation** (2.2.7): + 100 to + 104 (dried substance).

Dissolve 0.100 g in ethanol \( R \) and dilute to 10.0 ml with the same solvent.

**Related substances.** Liquid chromatography (2.2.29). Carry out the test protected from light.

**Test solution.** Dissolve 25.0 mg of the substance to be examined in acetonitrile \( R \) and dilute to 10.0 ml with the same solvent.

**Reference solution (a).** Dissolve 2.5 mg of fluocinolone acetonide CRS and 2.5 mg of triamcinolone acetonide CRS in 45 ml of acetonitrile \( R \) and dilute to 100.0 ml with water \( R \).

**Reference solution (b).** Dilute 1.0 ml of the test solution to 100.0 ml with acetonitrile \( R \).

**Column**:  
- size: \( l = 0.25 \, \text{m}, \theta = 4.6 \, \text{mm} \),
- stationary phase: base-deactivated end-capped octadecylsilyl silica gel for chromatography \( R \) (5 µm).

**Mobile phase**: mix 450 ml of acetonitrile \( R \) with 500 ml of water \( R \) and allow to equilibrate; adjust the volume to 1000.0 ml with water \( R \) and mix again.

**Flow rate**: 1 ml/min.

**Injection**: 20 µl.

**Run time**: 4 times the retention time of fluocinolone acetonide.

**Retention times**: triamcinolone acetonide = about 8.5 min; fluocinolone acetonide = about 10 min.

**System suitability**:  
- resolution: minimum of 3.0 between the peaks due to triamcinolone acetonide and fluocinolone acetonide in the chromatogram obtained with reference solution (a).

**Limits**:  
- any impurity: not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (1 per cent) and not more than 1 such peak has an area greater than half the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent),
- total: not more than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (2.5 per cent),
- disregard limit: 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

**Loss on drying** (2.2.32): maximum 1.0 per cent, determined on 1.000 g by drying in an oven at 105 °C for 3 h.

**ASSAY**

**Protect the solutions from light throughout the assay.**

Dissolve 50.0 mg in alcohol \( R \) and dilute to 50.0 ml with the same solvent. Dilute 2.0 ml of this solution to 100.0 ml with alcohol \( R \). Measure the absorbance (2.2.25) at the maximum at 238 nm.

Calculate the content of C\textsubscript{24}H\textsubscript{30}F\textsubscript{2}O\textsubscript{6} taking the specific absorbance to be 355.

**STORAGE**

Protected from light.