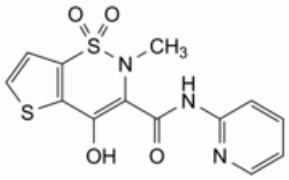
Edition: BP 2025 (Ph. Eur. 11.6 update)

Tenoxicam

General Notices

(Ph. Eur. monograph 1156)



$C_{13}H_{11}N_3O_4S_2$ 337.4 *59804-37-4*

Action and use

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

Preparations

Tenoxicam Injection

Tenoxicam Tablets

Ph Eur

DEFINITION

4-Hydroxy-2-methyl-*N*-(pyridin-2-yl)-2*H*-thieno[2,3-*e*]1,2-thiazine-3-carboxamide 1,1-dioxide.

Content

99.0 per cent to 101.0 per cent (anhydrous substance).

CHARACTERS

Appearance

Yellow, crystalline powder.

Solubility

Practically insoluble in water, sparingly soluble in methylene chloride, very slightly soluble in anhydrous ethanol. It dissolves in solutions of acids and alkalis.

It shows polymorphism (*5.9*).

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison *tenoxicam CRS*.

If the spectra obtained in the solid state show differences, dissolve the substance to be examined and the reference substance separately in the minimum volume of *methylene chloride R*, evaporate to dryness and record new spectra using the residues.

TESTS

Appearance of solution

The solution is clear (2.2.1).

Dissolve 0.10 g in *methylene chloride R* and dilute to 20 mL with the same solvent.

Related substances

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

Solvent mixture Mix equal volumes of *acetonitrile R* and *water R*. Adjust to apparent pH 3.2 with *dilute phosphoric acid R1*.

Test solution Dissolve 35 mg of the substance to be examined in the solvent mixture, sonicate and dilute to 50.0 mL with the solvent mixture.

Reference solution (a) Dilute 1.0 mL of the test solution to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

Reference solution (b) Dissolve 7 mg of pyridin-2-amine R (impurity A) in the solvent mixture and dilute to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 100.0 mL with the solvent mixture.

Reference solution (c) Dissolve the contents of a vial of *tenoxicam impurity mixture CRS* (impurities B, G and H) in 1.0 mL of the test solution.

Column:

— *size*: *l* = 0.15 m, Ø = 4.6 mm;

— *stationary phase*: diisopropylcyanosilyl silica gel for chromatography R (3.5 µm);

— *temperature*: 35 °C.

Mobile phase:

— *mobile phase A*: mix 25 volumes of *methanol R2* and 75 volumes of *water for chromatography R* and adjust to apparent pH 3.2 with *dilute phosphoric acid R1*;

— *mobile phase B*: mix 25 volumes of *water for chromatography R* and 75 volumes of *methanol R2* and adjust to apparent pH 3.2 with *dilute phosphoric acid R1*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 5	96	4
5 - 16	96 → 76	4 → 24
16 - 25	76	24

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 230 nm.

Injection 20 µL.

Identification of impurities:

— use the chromatogram obtained with reference solution (b) to identify the peak due to impurity A;

— use the chromatogram supplied with *tenoxicam impurity mixture CRS* and the chromatogram obtained with reference solution (c) to identify the peaks due to impurities B, G and H; for identification of impurities G and H, which may be inverted in the elution order, take into account the heights of the corresponding peaks in the chromatogram supplied with *tenoxicam impurity mixture CRS*.

Relative retention With reference to tenoxicam (retention time = about 12 min): impurity A = about 0.1; impurity G = about 0.85; impurity H = about 0.9; impurity B = about 1.3.

System suitability Reference solution (c):

— *resolution*: minimum 1.3 between the peaks due to impurity H (or G if peaks are inverted) and tenoxicam, and between the peaks due to impurities G and H; if necessary, optimise the apparent pH of the mobile phases within the range 3.0-3.4.

Limits:

— *correction factors*: for the calculation of content, multiply the peak areas of the following impurities by the corresponding correction factor: impurity A = 0.2; impurity B = 2.0;

— *impurities A, B*: for each impurity, not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.15 per cent);

— *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);

— *total*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 per cent);

— *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Water (*2.5.12*)

Maximum 0.5 per cent, determined on 1.000 g.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.250 g in 5 mL of *anhydrous formic acid R*. Add 70 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 33.74 mg of $C_{13}H_{11}N_3O_4S_2$.

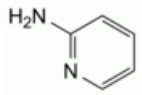
STORAGE

Protected from light.

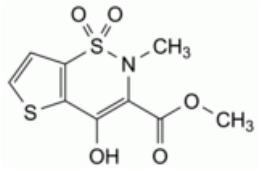
IMPURITIES

Specified impurities *A, B.*

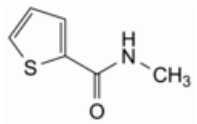
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) C, D, E, F, G, H.



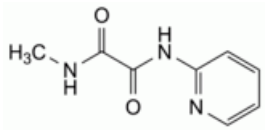
A. pyridin-2-amine,



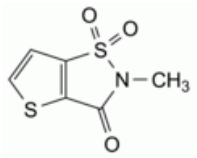
B. methyl 4-hydroxy-2-methyl-2*H*-thieno[2,3-*e*]1,2-thiazine-3-carboxylate 1,1-dioxide,



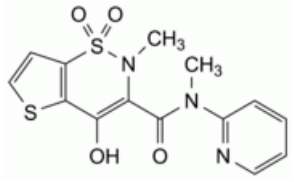
C. *N*-methylthiophene-2-carboxamide,



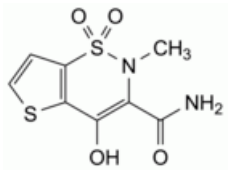
D. *N*-methyl-*N*′-(pyridin-2-yl)-ethanediamide,



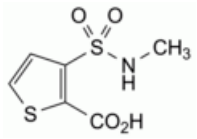
E. 2-methylthieno[2,3-*d*]isothiazol-3(2*H*)-one 1,1-dioxide,



F. 4-hydroxy-*N*,2-dimethyl-*N*-(pyridin-2-yl)-2*H*-thieno[2,3-*e*]1,2-thiazine-3-carboxamide 1,1-dioxide,



G. 4-hydroxy-2-methyl-2*H*-thieno[2,3-*e*]1,2-thiazine-3-carboxamide 1,1-dioxide,



H. 3-[(methylamino)sulfonyl]thiophene-2-carboxylic acid.

Ph Eur