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

Ketoprofen Capsules

General Notices

Action and use

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

DEFINITION

Ketoprofen Capsules contain Ketoprofen.

The capsules comply with the requirements stated under Capsules and with the following requirements.

Content of ketoprofen, $C_{16}H_{14}O_3$

92.5 to 107.5% of the stated amount.

IDENTIFICATION

Shake a quantity of the contents of the capsules containing 0.5 g of Ketoprofen with 50 mL of *chloroform* for 5 minutes, filter, evaporate to dryness using a rotary evaporator and induce crystallisation by prolonged scratching of the side of the container with a glass rod. The *infrared absorption spectrum* of the crystals, Appendix II A, is concordant with the *reference spectrum* of ketoprofen *(RS 198)*.

TESTS

Dissolution

Comply with the requirements for Monographs of the British Pharmacopoeia in the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of a *phosphate buffer* prepared by dissolving 1.46 g of *potassium dihydrogen orthophosphate* and 20.06 g of *disodium hydrogen orthophosphate* in sufficient *water* to produce 1000 mL, adjusting the pH to 7.5 if necessary with *orthophosphoric acid*, at a temperature of 37 ± 0.5°, as the medium.

PROCEDURE

After 45 minutes withdraw a sample of the medium, filter and dilute the filtrate with sufficient of the dissolution medium to give a solution expected to contain about 0.001% w/v of Ketoprofen. Measure the *absorbance* of the filtered sample at the maximum at 260 nm, Appendix II B, using dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of ketoprofen, $C_{16}H_{14}O_3$, in the medium taking 662 as the value of A(1%, 1 cm) at the maximum at 260 nm.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions freshly prepared in solvent A.

Solvent A A mixture of 40 volumes of *acetonitrile* and 60 volumes of *water*.

(1) Shake a quantity of the contents of the capsules containing 0.1 g of Ketoprofen in 100 mL, filter and use the filtrate.
(2) Dilute 1 volume of solution (1) to 50 volumes. Further dilute 1 volume of this solution to 10 volumes.
(3) 0.0002% w/v of *ketoprofen impurity C EPCRS*.
(4) 0.0003% w/v of *ketoprofen impurity A EPCRS*.
(5) Dilute 1 volume of solution (1) to 100 volumes. To 1 volume of this solution add 1 volume of solution (4).
(6) Dilute 1 volume of solution (2) to 10 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Nucleosil C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 233 nm.
(f) Inject 20 µL of each solution.
(g) Allow the chromatography to proceed for seven times the retention time of ketoprofen.

MOBILE PHASE

2 volumes of freshly prepared *phosphate buffer pH 3.5*, 43 volumes of *acetonitrile* and 55 volumes of *water*.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to ketoprofen (retention time about 8 minutes) are: impurity C, about 0.3 and impurity A, about 1.6.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (5), the *resolution* between the peaks due to ketoprofen and impurity A is at least 7.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity A is not greater than the area of the principal peak in the chromatogram obtained with solution (4) (0.3%);

the area of any peak corresponding to impurity C is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (0.2%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of all the *secondary peaks* excluding impurities A and C is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (6) (0.02%).

ASSAY

Shake a quantity of the mixed contents of 20 capsules containing 50 mg of Ketoprofen for 10 minutes with 300 mL of *methanol (75%)*, mix and dilute to 500 mL with *methanol (75%)*. Allow to stand, dilute 5 mL of the supernatant liquid to 100 mL with *methanol (75%)* and measure the *absorbance* of the resulting solution at the maximum at 258 nm, Appendix II B. Calculate the content of $C_{16}H_{14}O_3$ taking 662 as the value of A(1%, 1 cm) at the maximum at 258 nm.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A and C listed under Ketoprofen.