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

Ketoprofen Gel

General Notices

Action and use

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

DEFINITION

Ketoprofen Gel is a solution of Ketoprofen in a suitable water-miscible basis.

The gel complies with the requirements stated under Topical Semi-solid Preparations and with the following requirements.

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

92.5 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the gel containing 60 mg of Ketoprofen with 10 mL of *dichloromethane* and filter. Evaporate the filtrate to dryness under nitrogen. Dry the residue at 60° for 1 hour. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of ketoprofen (*RS 484*).

TESTS

Acidity or alkalinity

pH of a 1% w/v dispersion of the gel in *carbon dioxide-free water*, 5.0 to 7.5, Appendix V L.

Ketoprofen ethyl ester

In the Assay, in the chromatogram obtained with solution (1) the area of any peak corresponding to ketoprofen ethyl ester is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (4.0%).

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared immediately before use.

(1) Dilute a quantity of the gel containing 10 mg of Ketoprofen with sufficient *methanol* to produce a solution containing 0.01% w/v of Ketoprofen.
(2) Dilute 1 volume of solution (1) to 100 volumes with *methanol*.
(3) 0.00002% w/v of *ketoprofen impurity A EPCRS* in the mobile phase.
(4) 0.00002% w/v of *ketoprofen impurity C EPCRS* in the mobile phase.
(5) 0.0005% w/v of *ketoprofen BPCRS* and 0.0001% w/v of *ketoprofen impurity A EPCRS* in *methanol*.

(6) Dilute 1 volume of solution (2) to 10 volumes with *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) with a specific surface area of 350 m^2/g and a pore size of 10 nm (Nucleosil 100 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 7 times the retention time of ketoprofen.

MOBILE PHASE

2 volumes of freshly prepared *phosphate buffer solution 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; impurity E, about 0.7; impurity B, about 0.8; impurity D, about 1.5; impurity A, about 1.6; impurity F, about 2.3.

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

Use the chromatogram obtained with solution (3) to identify the peak due to impurity A; use the chromatogram obtained with solution (4) to identify the peak due to impurity C.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity A is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (3) (0.5%);

the area of any peak corresponding to impurity C is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (4) (0.5%);

the area of any peak corresponding to impurity B, D, E or F is not greater than half the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the area of any other *secondary peak* is not greater than 0.2 times 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) (2.5%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (6) (0.1%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared with solution A.

Solution A 270 mL of *acetonitrile* and 550 mL of a 0.5% w/v solution of *ammonium acetate*.

(1) Shake a weighed quantity of the gel containing 10 mg of Ketoprofen with 50 mL of *methanol* for 15 minutes, centrifuge the mixture for 5 minutes, and dilute 25 mL of the supernatant liquid with sufficient solution A to produce 100 mL.
(2) Add 19 mL of *methanol* to 5 mL of a 0.1% w/v solution of *ketoprofen BPCRS* in *methanol*, add sufficient solution A to produce 100 mL and mix.
(3) Add 19 mL of *methanol* to 5 mL of a 0.004% w/v solution of *ketoprofen ethyl ester BPCRS* in *methanol*, add sufficient solution A to produce 100 mL and mix.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Spherisorb ODS 1 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 254 nm.
(f) Inject 20 µL of each solution.
(g) Allow the chromatography to proceed for 8 times the retention time of ketoprofen.

MOBILE PHASE

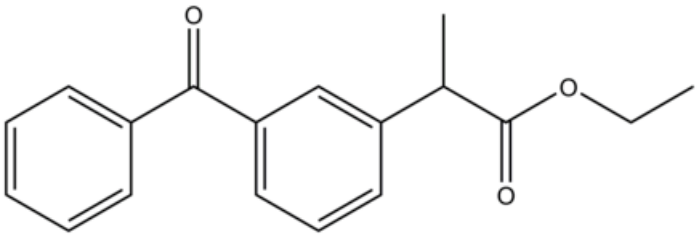
450 volumes of a solution containing 40% v/v of *methanol* and 60% v/v of *acetonitrile* and 550 volumes of a 0.5% w/v solution of *ammonium acetate*, adjusted to pH 5.9 by the addition of 10% w/w *nitric acid*.

DETERMINATION OF CONTENT

Calculate the content of $C_{16}H_{14}O_3$ in the gel using the declared content of $C_{16}H_{14}O_3$ in *ketoprofen BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Ketoprofen and:



1. ethyl 2-(3-benzoylphenyl)propionate (ketoprofen ethyl ester).