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Ketoprofen Solution for Use in Drinking Water

General Notices

Action and use

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

DEFINITION

Ketoprofen Solution for Use in Drinking Water is a solution of Ketoprofen in a suitable vehicle.

The solution complies with the requirements stated under Oral Liquids and with the following requirements.

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

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Extract a volume of the solution containing 0.1 g of Ketoprofen, with two 5-mL quantities of *dichloromethane*. Retain and combine the lower layers, filter and evaporate to dryness under nitrogen. Dry the residue at 60° for 60 minutes. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of ketoprofen (*RSV 053*).

TESTS

Related substances

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

(1) Dilute a quantity of the solution with sufficient mobile phase to produce a solution containing 0.1% w/v of Ketoprofen.
(2) Dilute 1 volume of solution (1) to 100 volumes. Further dilute 1 volume to 5 volumes.
(3) 0.0002% w/v of *ketoprofen impurity A EPCRS*.
(4) 0.0002% w/v of *ketoprofen impurity C EPCRS*.
(5) 0.0005% w/v of *ketoprofen BPCRS* and 0.0001% w/v of *ketoprofen impurity A EPCRS*.

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 2.2.

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):

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.

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 (3) (0.2%);

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 (4) (0.2%);

the area of any peak corresponding to impurity B, D, E or F is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the area of any other *secondary peak* is not greater than 5 times the area of the principal peak in the chromatogram obtained with solution (2) (1.0%);

the sum of the areas of all the *secondary peaks* excluding impurities A and C is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (0.4%).

Disregard any peak (excluding impurities A, B, C, D, E and F) with an area less than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in mobile phase.

(1) Dilute a weighed quantity of the solution with sufficient mobile phase to produce a solution containing 0.001% w/v of Ketoprofen.
(2) 0.001% w/v of *ketoprofen BPCRS*.
(3) 0.0005% w/v of *ketoprofen BPCRS* and 0.0001% w/v of *ketoprofen impurity A EPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to ketoprofen and impurity A is at least 7.0.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the solution, Appendix V G, and calculate the content of $C_{16}H_{14}O_3$, weight in volume in the solution 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.