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

Nabumetone Oral Suspension

General Notices

Action and use

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

DEFINITION

Nabumetone Oral Suspension contains Nabumetone in a suitable flavoured vehicle.

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

Content of nabumetone, $C_{15}H_{16}O_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Add a volume of the well-shaken suspension containing 0.1 g of Nabumetone to 10 mL of *dichloromethane*, shake, allow to separate and use the lower layer.
(2) 1.0% w/v of *nabumetone BPCRS* in *dichloromethane*.
(3) A mixture of equal volumes of solutions (1) and (2).

CHROMATOGRAPHIC CONDITIONS

(a) Use a silica gel GF_{254} precoated plate (Merck 5715 plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 2 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air and examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

dichloromethane

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) is similar in position and colour to the spot in the chromatogram obtained with solution (2) and the chromatogram obtained with solution (3) shows a single, compact spot at the same Rf value as the spot in the chromatogram obtained with solution (2).

B. In the Assay the retention time of the principal peak in the chromatogram obtained with solution (1) is the same as that of the peak in the chromatogram obtained with solution (2).

TESTS

Related substances

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

(1) Shake a volume of the suspension containing 0.5 g of Nabumetone with 10 mL of *methanol* until completely dispersed, add sufficient *acetonitrile* to produce 100 mL, shake for a further 5 minutes and filter (Whatman No. 1 paper is suitable).
(2) Dilute 1 volume of solution (1) to 200 volumes.
(3) 0.0015% w/v of *nabumetone impurity F EPCRS* in *acetonitrile*.
(4) 0.002% w/v of each of *nabumetone BPCRS* and *nabumetone impurity D BPCRS* in *acetonitrile*.
(5) Dilute 1 volume of solution (2) to 10 volumes with *acetonitrile*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *base-deactivated octadecylsilyl silica gel for chromatography* (4 µm) (Genesis C18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 254 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A 12 volumes of *tetrahydrofuran*, 28 volumes of *acetonitrile* and 60 volumes of a 0.1% v/v solution of *glacial acetic acid* in *carbon dioxide-free water*.

Mobile phase B 24 volumes of *tetrahydrofuran*, 56 volumes of *acetonitrile* and 20 volumes of a 0.1% v/v solution of *glacial acetic acid* in *carbon dioxide-free water*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-12	100	0	isocratic
12-28	100→0	0→100	linear gradient
28-33	0	100	isocratic
33-34	0→100	100→0	linear gradient
34-35	100	0	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to nabumetone (retention time about 11 minutes) are: impurity D, about 1.1 and impurity F, about 2.7.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the two principal peaks is at least 1.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity F is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (0.3%);

the area of any other *secondary peak* is not greater than 0.4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of any other *secondary peaks* is not greater than 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 (5) (0.05%).

ASSAY

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

(1) To a weighed quantity of the suspension containing 0.1 g of Nabumetone, add 70 mL of *ethanol (96%)*, mix with the aid of ultrasound for 45 minutes, add sufficient *ethanol (96%)* to produce 100 mL and filter (Whatman GF/C paper is suitable). Dilute 1 volume of the filtrate to 20 volumes with the mobile phase.
(2) Dilute 1 volume of a 0.1% w/v solution of *nabumetone BPCRS* in *acetonitrile* to 20 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *base-deactivated octadecylsilyl silica gel for chromatography* (4 µm) (Genesis 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 254 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

18 volumes of *tetrahydrofuran*, 40 volumes of a 0.1% v/v solution of *glacial acetic acid* in *carbon dioxide-free water* and 42 volumes of *acetonitrile*.

When the chromatograms are recorded under the prescribed conditions the retention time of nabumetone is about 4 minutes.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the oral suspension, Appendix V G, and calculate the content of $C_{15}H_{16}O_2$, weight in volume, from the chromatograms obtained using the declared content of $C_{15}H_{16}O_2$ in *nabumetone BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Nabumetone.