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

Ibuprofen Effervescent Granules

General Notices

Action and use

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

DEFINITION

Ibuprofen Effervescent Granules contain Ibuprofen in a suitable effervescent basis.

The granules comply with the requirements stated under Granules and with the following requirements.

Content of ibuprofen, $C_{13}H_{18}O_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Extract a quantity of the powdered granules containing 0.5 g of Ibuprofen with 20 mL of *acetone*, filter and evaporate the filtrate to dryness. Wash the residue with 20 mL of *water*, filter, and discard the filtrate. Wash the resulting residue with 20 mL of *acetone*, and evaporate to dryness. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of ibuprofen (*RS 186*).

TESTS

Related substances

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

(1) Mix with the aid of ultrasound a quantity of the powdered granules containing 0.2 g of Ibuprofen with 20 mL of mobile phase A. Add sufficient mobile phase A to produce 100 mL and filter (Whatman GF/C is suitable).
(2) Dilute 1 volume of solution (1) to 100 volumes with mobile phase A. Further dilute 1 volume to 10 volumes with mobile phase A.
(3) Dissolve 20 mg of *ibuprofen BPCRS* in 2 mL of *acetonitrile R1* , add 1 mL of a 0.006% w/v solution of *ibuprofen impurity B BPCRS* in *acetonitrile R1* and dilute to 10 mL with mobile phase A.
(4) 0.0006% w/v of *4'-isobutylacetophenone BPCRS* (impurity E) in mobile phase A.
(5) Dissolve the contents of a vial of *ibuprofen for peak identification EPCRS* in 1 mL of *acetonitrile R1* and dilute to 5 mL with mobile phase A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped octadecylsilyl amorphous organosilica polymer for chromatography* (5 µm) (XTerra MS C18 is suitable).
(b) Use gradient 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 214 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A 0.5 volume of *orthophosphoric acid*, 340 volumes of *acetonitrile R1* and sufficient *water* to produce 1000 volumes.

Mobile phase B 0.5 volume of *orthophosphoric acid*, 100 volumes of *water* and sufficient *acetonitrile R1* to produce 1000 volumes.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-25	100	0	isocratic
25-55	100→0	0→100	linear gradient
55-70	0	100	isocratic
70-71	0→100	100→0	linear gradient
71-85	100	0	re-equilibration

When chromatograms are recorded under the prescribed conditions, the relative retentions with reference to ibuprofen (retention time about 26 minutes) are: impurity J, about 0.18; impurity N, about 0.3; impurity A, about 0.9; impurity B, about 1.08 and impurity E, about 1.11.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *peak-to-valley ratio* is at least 5.0, where *Hp* is the height above the baseline of the peak due to impurity B and *Hv* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to ibuprofen.

LIMITS

Use the chromatogram supplied with *ibuprofen for peak identification EPCRS* and the chromatogram obtained with solution (5) to identify the peaks due to impurities A, J, and N. Use the chromatogram obtained with solution (4) to identify the peaks due to impurity E.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity E is not greater than 3 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%);

the area of any peak corresponding to impurity A, J or N is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.15% of each);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.1%);

the sum of the areas of any *secondary peaks* is not greater than 7 times the area of the principal peak in the chromatogram obtained with solution (2) (0.7%).

Disregard any peak with an area less than half the area of the principal peak in the chromatogram obtained with solution (2) (0.05%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in a mixture of 35 volumes of 0.1 % w/v of *formic acid* and 65 volumes of *methanol* (solution A).

(1) Shake a quantity of the powdered granules containing 3 g of Ibuprofen with 500 mL of solution A. Add sufficient solution A to produce 1000 mL and mix thoroughly. Filter the solution (a Whatman GF/C 1.2-µm filter is suitable) and dilute 0.5 volume of the filtrate to 15 volumes.
(2) 0.01% w/v of *ibuprofen BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (10 µm) (Nucleosil C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 264 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

3 volumes of *orthophosphoric acid*, 247 volumes of *water* and 750 volumes of *methanol*.

When the chromatograms are recorded under the prescribed conditions, the retention time of ibuprofen is about 7 minutes.

DETERMINATION OF CONTENT

Calculate the content of ibuprofen, $C_{13}H_{18}O_2$, in the granules from the chromatograms obtained and using the declared content of $C_{13}H_{18}O_2$ in *ibuprofen BPCRS*.

IMPURITIES

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