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Ibuprofen Prolonged-release Capsules

General Notices

Prolonged-release Ibuprofen Capsules

Ibuprofen Prolonged-release Capsules from different manufacturers, whilst complying with the requirements of the monograph, are not interchangeable unless otherwise justified and authorised.

Action and use

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

DEFINITION

Ibuprofen Prolonged-release Capsules contain Ibuprofen. They are formulated so that the medicament is released over a period of several hours.

PRODUCTION

A suitable dissolution test is carried out to demonstrate the appropriate release of Ibuprofen. The dissolution profile reflects the *in vivo* performance which in turn is compatible with the dosage schedule recommended by the manufacturer.

The capsules comply with the requirements stated under Capsules 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 capsule contents containing 0.5 g of Ibuprofen with 20 mL of *acetone*, filter and evaporate the filtrate to dryness in a current of air without heating. 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) Disperse a quantity of the capsule contents containing 0.2 g of Ibuprofen with 20 mL of *acetonitrile R1*, 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 0.2; 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 peak due to impurity E.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to ibuprofen 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 0.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.05%).

ASSAY

Weigh the contents of 20 capsules. Mix, and powder if necessary. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Shake a quantity of the capsule contents containing 0.1 g of Ibuprofen in 50 mL of the mobile phase, add sufficient mobile phase to produce 100 mL and mix. Centrifuge and dilute 1 volume of the supernatant liquid to 10 volumes with the mobile phase.
(2) 0.01% w/v of *ibuprofen BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *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 capsules 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.