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Ibuprofen Gel

General Notices

Details for the public consultation of this monograph are as follows:

EAG/Panel/Working Party	Medicinal Chemicals 2
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Deadline for Comment	31st March 2025
Target Publication Date (subject to change)	BP 2026
Notes	Revised monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. **T: Identification**IR replaced with HPLC DAD, harmonised with Ibuprofen injection. **T: Related substances** Limit for impurity 1 has been included, solutions have been adjusted to accommodate amended impurity profile & identification of impurity 1, quantitative limits have been introduced. **T: Impurities** Ibuprofen alcohol esters added as impurities 1, 2 and 3. Impurity F excluded as this is not controlled by the rel subs method

Action and use

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

DEFINITION

Ibuprofen Gel is a solution of Ibuprofen 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 ibuprofen, $C_{13}H_{18}O_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 210 to 400 nm.

The UV spectrum of the principal peak in the chromatogram obtained with solution (1) is concordant with that of the peak in the chromatogram obtained with solution (2);

the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

TESTS

Acidity or alkalinity

The pH of the gel is 5.5 to 7.5, Appendix V L.

Related substances

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

(1) Disperse with the aid of ultrasound a quantity of the gel containing 0.2 g of Ibuprofen in 50 mL of mobile phase A, dilute to 100 mL with mobile phase A and filter (Whatman GF/C filter is suitable).
(2) Dilute 1 volume of solution (1) to 200 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.
(6) 2% w/v of *ibuprofen BPCRS* in *industrial methylated spirit* and allow to stand for 1 hour. Dilute 1 volume to 10 volumes with mobile phase A (generation of impurity 1).
(7) Dilute 1 volume of solution (2) to 5 volumes 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

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.

CALCULATION OF IMPURITIES

For each impurity, use the concentration of ibuprofen in solution (2).

For the reporting threshold, use the concentration of ibuprofen in solution (7).

For peak identification, use solutions (4), (5) and (6).

Ibuprofen retention time: about 26 minutes.

Relative retention: impurity J, about 0.2; impurity N, about 0.3; impurity A, about 0.9; impurity B, about 1.08, impurity E, about 1.11 and impurity 1, about 1.4.

LIMITS

- impurity 1: not more than 0.5%;
- impurity E: not more than 0.3%;
- impurities A, J and N: not more than 0.15% of each;
- unspecified impurities: for each impurity, not more than 0.1%;
- total impurities (excluding impurity 1): not more than 0.7%;
- reporting threshold: 0.05%.

ASSAY

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

(1) Disperse with the aid of ultrasound a weighed quantity of the gel containing 50 mg of Ibuprofen in 50 mL of *methanol*, dilute to 100 mL with *methanol* and filter (Whatman GF/C filter is suitable). Dilute 1 volume to 2 volumes with the mobile phase.
(2) 0.05% w/v of *ibuprofen BPCRS* in *methanol*. Dilute 1 volume to 2 volumes with the mobile phase.

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 $C_{13}H_{18}O_2$ in the gel 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, excluding impurity F, and:

 1. [systematic impurity name (ibuprofen ethyl ester)]

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 2. [systematic impurity name (ibuprofen methyl ester)]

2. [systematic impurity name (ibuprofen methyl ester)]

 3. [systematic impurity name (ibuprofen propyl ester)]

3. [systematic impurity name (ibuprofen propyl ester)]