

Draft Proposal for Comments and Inclusion in The Indian Pharmacopoeia

Ibuprofen Oral Suspension

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This draft proposal contains monograph text for inclusion in the Indian Pharmacopoeia (IP). The content of this draft document is not final, and the text may be subject to revisions before publication in the IP. This draft does not necessarily represent the decisions or the stated policy of the IP or Indian Pharmacopoeia Commission (IPC).

Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Document History and Schedule for the Adoption Process

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Further follow-up action as required.	

Ibuprofen Oral Suspension

Ibuprofen Oral Suspension contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Ibuprofen, C₁₃H₁₈O₂.

Usual strength. ~~50 mg per 5 ml;~~ 100 mg per 5 ml.

Identification

Shake a quantity of the suspension containing ~~0.5~~ 0.1 g of Ibuprofen with 25 ml of *dichloromethane* and 15 ml *water*. Allow to stand until the layers have separated and discard the upper layer. Shake the lower layer with 5 ml of *water* and discard the upper layer and evaporate the lower layer to dryness in a current of air without heating. ~~Evaporate the lower layer to dryness;~~ add 20 ml of *water* to the residue and filter. Wash the residue with 20 ml of *dichloromethane* and evaporate to dryness in a current of air without heating. The residue complies with the following test,

Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *ibuprofen IPRS* or with the reference spectrum of *ibuprofen*.

Tests

pH (2.4.24). 3.6 to 4.6.

Dissolution (2.5.2).

Apparatus No. 2 (Paddle),
Medium. 900 ml of *phosphate buffer pH 7.2*,
Speed and time. 50 rpm and 30 minutes.

Note- Shake the oral suspension for 30 seconds and place a one dose volume of the oral suspension in to each dissolution vessel.

~~Shake the oral suspension for 30 seconds and place a volume of the oral suspension containing 0.2 g of Ibuprofen in to each dissolution vessel.~~

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Test solution. Dilute the filtrate, if necessary, with the dissolution medium.

Reference solution (a). ~~A 0.0011 per cent w/v solution~~ A 0.0022 per cent w/v solution of *ibuprofen IPRS* in the dissolution medium.

Reference solution (b). A solution containing 0.03 per cent w/v, each of, *benzophenone* and *ibuprofen IPRS* in the dissolution medium.

Chromatographic system

- a stainless steel column 15 cm × 4.6 mm, packed with octylsilane bonded to porous silica (5 μm),
- mobile phase: a mixture of 63 volume of 0.01 M *orthophosphoric acid* and 37 volumes of *acetonitrile*,
- flow rate: 2 ml per minute,
- spectrophotometer set at 220 nm,
- injection volume: 10 μl.

Inject reference solution (b). The test is not valid unless the resolution between the peaks due to *benzophenone* and *ibuprofen* is not less than 1.5.

Inject reference solution (a) and the test solution.

Calculate the content of C₁₃H₁₈O₂ in the medium.

D. Not less than 75 per cent of the stated amount of C₁₃H₁₈O₂.

~~pH (2.4.24) 3.6 to 4.6~~

Related substances. Determine by liquid chromatography (2.4.14).

Test solution. Disperse a quantity of oral suspension containing 0.2 g of Ibuprofen in 20 ml of *acetonitrile* with the aid of ultrasound and dilute to 100.0 ml with mobile phase A.

Reference solution (a). A 0.0002 per cent w/v solution of *ibuprofen IPRS* in the mobile phase A.

Reference solution (b). Dissolve 20 mg of *ibuprofen IPRS* in 2.0 ml of *acetonitrile*, add 1 ml of a 0.006 per cent w/v solution of *ibuprofen impurity B IPRS* in *acetonitrile* and dilute to 10.0 ml with mobile phase A.

Reference solution (c). ~~A solution containing 0.003 per cent w/v, each of, A 0.0015 per cent w/v solution of, each of, *ibuprofen impurity A IPRS*, *ibuprofen impurity J IPRS* and *ibuprofen impurity N IPRS* in *acetonitrile*.~~ Dilute 1.0 ml of the solution to 10.0 ml with mobile phase A.

Reference solution (d). A 0.0006 per cent w/v solution of *ibuprofen impurity E IPRS* (4'-*isobutylacetophenone*) in mobile phase A.

Chromatographic system

- a stainless steel column 15 cm x 4.6 mm, packed with end-capped octadecylsilane amorphous organosilica polymer (5 µm), (Such as XTerra MS C18),
- mobile phase: A. a mixture of 34 volumes of *acetonitrile*, 66 volumes of *water* and 0.05 volume of *orthophosphoric acid*,
B. a mixture of 10 volumes of *water*, 90 volumes of *acetonitrile* and 0.05 volume of *orthophosphoric acid*,
- a gradient programme using the conditions given below,
- flow rate: 2 ml per minute,
- spectrophotometer set at 214 nm,
- injection volume: 20 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	100	0
25	100	0
55	0	100
70	0	100
71	100	0
85	100	0

Name	Relative retention time
Ibuprofen impurity J ¹	0.2
Ibuprofen impurity N ²	0.3
Ibuprofen impurity A ³	0.9
Ibuprofen (Retention time: about 26 minutes)	1.0
Ibuprofen impurity B ⁴	1.08
Ibuprofen impurity E ⁵	1.11

¹(2RS)-2-[4-(2-methylpropanoyl)phenyl]propanoic acid,

²(2RS)-2-(4-ethylphenyl)propanoic acid,

³(2RS)-2-[3-(2-methylpropyl)phenyl]propanoic acid,

⁴(2RS)-2-(4-butylphenyl)propanoic acid,

⁵4-*isobutylacetophenone*.

~~¹4-(2-methylpropyl)phenyl]ethanone.~~

Inject reference solution (c) and (d) to identify the peaks due to ibuprofen impurity A, ibuprofen impurity J, ibuprofen impurity N and ibuprofen impurity E, respectively.

Inject reference solution (b). The test is not valid unless the peak-to-valley ratio (H_p/H_v) is not less than 5.0, where H_p is the height above the baseline of the peak due to ibuprofen and H_v is the height above the baseline of the lowest point of the curve separating this peak from the peak due to ibuprofen impurity B.

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to Ibuprofen impurity E is not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 per cent), the area of any peak corresponding to Ibuprofen impurity A, Ibuprofen impurity J and Ibuprofen impurity N, each of, is not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.15 per cent), the area of any other secondary peak is not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent) and the sum of areas of any secondary peaks is not more than 7 times of the area of the principal peak in the chromatogram obtained with reference solution (a) (0.7 per cent). Ignore any peak with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Other tests. Comply with the tests stated under Oral Liquids.

Assay. Determine by liquid chromatography (2.4.14).

Test solution. Disperse a quantity of oral suspension containing 0.1 g of Ibuprofen in 40 ml of *acetonitrile* and add 10 ml of 0.01 M *orthophosphoric acid*, shake vigorously and dilute to 100.0 ml with 0.01 M *orthophosphoric acid*, filter.

Reference solution. A 0.1 per cent w/v solution of *ibuprofen IPRS* in the mobile phase.

Chromatographic system

- a stainless steel column 30 cm x 3.9 mm, packed with end-capped octadecylsilane bonded to porous silica (10 μm), (Such as $\mu\text{Bondapak C18}$),
- mobile phase: a mixture of 40 volumes of *acetonitrile* and 60 volumes of 0.01 M *orthophosphoric acid*,
- flow rate: 2 ml per minute,
- spectrophotometer set at 220 nm,
- injection volume: 10 μl .

Inject the reference solution. The test is not valid unless the relative standard deviation for replicate injections is not more than 2.0 per cent.

~~The retention time of ibuprofen is about 21 minutes.~~

Inject the reference solution and the test solution.

Determine the weight per ml of the oral suspension (2.4.29) and calculate the content of $\text{C}_{13}\text{H}_{18}\text{O}_2$ in the suspension.

Storage. Store protected from light, at a temperature not exceeding 30°.