Ibuprofen Oral Suspension

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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.

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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, $C_{13}H_{18}O_2$.

Usual strength. 100 mg per 5 ml.

Identification

Shake a quantity of the suspension containing 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, 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 one dose volume of the oral suspension 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 0.011 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 volumes 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 $C_{13}H_{18}O_2$ in the medium.

Q. Not less than 75 per cent of the stated amount of $C_{13}H_{18}O_2$.

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 mobile phase A.

Reference solution (b). Dissolve 20 mg of *ibuprofen IPRS* in 2 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, *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'-ibobutylacetophenone) 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,
[5]4-isobutylacetophenone.

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 (Hp/Hv) is not less than 5.0, where Hp is the height above the baseline of the peak due to ibuprofen and Hv 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 all other 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. Dissolve 25.0 mg of *ibuprofen IPRS* in 10 ml of *acetonitrile*, add 2.5 ml of *0.01 M orthophosphoric acid*, shake vigorously and dilute to 25.0 ml with *0.01 M orthophosphoric acid*.

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 µBondapak 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.

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 $C_{13}H_{18}O_2$ in the suspension.

Microbial contamination (2.2.9). Total aerobic viable count is not more than 10^3 CFU per g and total fungal count is not more than 10^2 CFU per g determined by plate count. 1 g is free from *Escherichia coli*.

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

DISSOLUTION AND ASSAY NEED TO BE VERIFIED