Bilastine Tablets

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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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Bilastine Tablets

Bilastine Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of bilastine, $C_{28}H_{37}N_3O_3$.

Usual strengths. 20 mg; 40 mg.

Identification

In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution.

Tests

Dissolution (2.5.2).
Apparatus No. 1 (Basket),
Medium. 500 ml of *0.1M hydrochloric acid*,
Speed and time. 100 rpm and 15 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Test solution. Use the filtrate, dilute if necessary, with the dissolution medium.

Reference solution. Dissolve a quantity of *bilastine IPRS* in 10 ml of *methanol* and dilute with the dissolution medium to obtain a solution containing 0.004 per cent w/v of bilastine.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Inertsil ODS 3V),
- column temperature: 40°,
- mobile phase: a mixture of 68 volumes of a buffer solution prepared by dissolving 1.74 g of *dipotassium hydrogen orthophosphate anhydrous* in 1000 ml of *water*, adjusted to pH 7.0 with *dilute orthophosphoric acid* and 32 volumes of *acetonitrile*,
- flow rate: 1.5 ml per minute,
- spectrophotometer set at 215 nm,
- injection volume: 50 µl.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{28}H_{37}N_3O_3$ in the medium.

Q. Not less than 80 per cent of the stated amount of $C_{28}H_{37}N_3O_3$.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 60 volumes of *water* and 40 volumes of *acetonitrile*.

Buffer solution. Dissolve 6.8 g of *potassium dihydrogen orthophosphate* and 2.5 g of *1-octane sulphonic acid sodium salt anhydrous* in 1000 ml of *water*, adjusted to pH 4.5 with *dilute orthophosphoric acid.*

Test solution. Disperse a quantity of powdered tablets containing 50 mg of Bilastine in the solvent mixture with the aid of ultrasound for 10 minutes with intermittent shaking and dilute to 100.0 ml with the solvent mixture, filter.

Reference solution (a). A 0.00025 per cent w/v solution of *bilastine IPRS* in the solvent mixture.

Reference solution (b). A solution containing 0.00025 per cent w/v of, each of, *bilastine impurity B IPRS* and *bilastine impurity F IPRS* and 0.05 per cent w/v of *bilastine IPRS* in the solvent mixture.

Reference solution (c). Dilute 1.0 ml of reference solution (a) solution to 10.0 ml with the solvent mixture.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Inertsil ODS 3V),
- column temperature: 40°,
- mobile phase: A. a mixture of 90 volumes of the buffer solution and 10 volumes of *acetonitrile*,

B. a mixture of 70 volumes of *acetonitrile* and 30 volumes of the buffer solution,

– a gradient programme using the conditions given below,
– flow rate: 1 ml per minute,
– spectrophotometer set at 215 nm,
– injection volume: 20 µl,

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	70	30
6	70	30
20	55	45
50	45	55
60	35	65
65	35	65
70	70	30
75	70	30

Name	Relative retention time	Correction factor
Bilastine impurity A[1*]	0.59	---
Bilastine impurity F[2]	0.85	0.99
Bilastine impurity B[3]	0.89	1.03
Bilastine	1.00	---
Bilastine impurity C[4*]	1.12	---
Bilastine impurity D[5*]	1.57	---
Bilastine impurity E[6*]	1.64	---

[*] Process impurity included for identification only and not to be included in the calculation of total degradation products,
[1]2-(4-(2-(4-(1-(2-hydroxyethyl)-1H-benzo[d]imidazol-2-yl)piperidine-1-yl)ethyl)phenyl)-2-methylpropanoic acid,
[2]2-(4-(2-(4-(1-(2-methoxyethyl)-1H-benzo[d]imidazol-2-yl)piperidine-1-yl)ethyl)phenyl)-2-methylpropanoic acid,
[3]1-(4-(2-carboxypropan-2-yl)phenethyl)-4-(1-(2-ethoxyethyl)-1H-benzo[d]imidazol-2-yl)piperidine 1-oxide.
[4]2-(4-(2-(4-(1-(2-ethoxyethyl)-1H-benzo[d]imidazol-2-yl)piperidine-1-yl)ethyl)phenyl)-N-(1-hydroxy-2-methylpropan-2-yl)-2-methylpropanamide,
[5]2-(4-(2-(4-(1-(2-ethoxyethyl)-1H-benzo[d]imidazole-2-yl)piperidine-1-yl)ethyl) phenyl) propan-2-yl)-4,4-dimethyl-4,5-dihydrooxazole,
[6] Methyl-2-(4-(2-(4-(1-(2-ethoxyethyl)-1H-benzo[d]imidazol-2-yl)piperidine-1-yl)ethyl)phenyl)-2-methylpropanoate,

Inject reference solution (a), (b) and (c). The test is not valid unless the resolution between the peaks due to bilastine impurity B and F is not less than 1.5 in the chromatogram obtained with reference solution (b), the column efficiency is not less than 2000 theoretical plates, the tailing factor is not more than 2.0, the relative standard deviation for replicate injections is not more than 5.0 per cent in the chromatogram obtained with reference solution (a) and the signal-to-noise ratio is not less than 10 in the chromatogram obtained with reference solution (c).

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to bilastine impurity B and F, each of, is not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 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) (0.5 per cent) and the sum of the areas of all the secondary peaks is not more than 4 times the area of the principal peak in the chromatogram obtained with reference solution (a) (2.0 per cent). Ignore any peak with an area less than 0.04 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.02 per cent).

Other tests. Comply with the tests stated under Tablets.

Assay. Determine by liquid chromatography (2.4.14).

Solvent mixture. 60 volumes of *water* and 40 volumes of *acetonitrile*.

Test solution. Weigh and powder 20 tablets. Disperse a quantity of the powder containing 0.1g of Bilastine in the solvent mixture with the aid of ultrasound for 10 minutes with intermittent shaking and dilute to 200.0 ml with the solvent mixture, filter. Dilute 5.0 ml of the filtrate to 25.0 ml with the solvent mixture.

Reference solution. A 0.01 per cent w/v solution of *bilastine IPRS* in the solvent mixture.

Chromatographic system

– a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Inertsil ODS 3V),

– column temperature: 40°,
– mobile phase: a mixture of 68 volumes of a buffer solution prepared by dissolve 1.74 g of *dipotassium hydrogen orthophosphate anhydrous* in 1000 ml of *water*, adjusted to pH 7.0 with *dilute orthophosphoric acid* and 32 volumes of *acetonitrile*,
– flow rate: 1.5 ml per minute,
– spectrophotometer set at 215 nm,
– injection volume: 20 µl.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{28}H_{37}N_3O_3$ in the tablets.

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