Desloratadine

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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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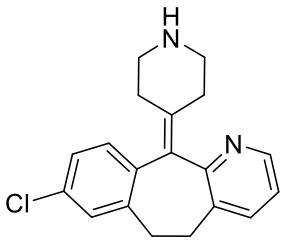
Desloratadine



$C_{19}H_{19}ClN_2$ Mol. Wt. 310.8

Desloratadine is Benzo[5,6]cyclohepta[1,2-*b*]pyridine, 8-chloro-6,11-dihydro-11-(4-piperidinylidene)-, 5*H*-;

Desloratadine contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{19}H_{19}ClN_2$, calculated on the anhydrous and solvent-free basis.

Category. Antihistamine.

Description. A white or almost white powder.

Identification

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

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

Tests

Related substances. *(Use test A, when the impurity profile includes desloratadine related compound B or fluorodesloratadine and use test B, when the impurity profile includes dechloro desloratadine, desloratadine related compound A or dehydrodesloratadine)*

A. Determine by liquid chromatography (2.4.14).

Test solution. Dissolve 40 mg of the substance under examination in mobile phase with the aid of ultrasound and dilute to 50.0 ml with mobile phase. Dilute 1.0 ml of the solution to 10.0 ml with the mobile phase.

Reference solution (a). A 0.008 per cent w/v solution of *desloratadine IPRS* in the mobile phase.

Reference solution (b). Dilute 1.0 ml of reference solution (a) to 100.0 ml with the mobile phase. Dilute 1.0 ml of the solution to 10.0 ml with the mobile phase.

Reference solution (c). A solution containing 0.008 per cent w/v of *desloratadine IPRS* and 0.00002 per cent w/v *desloratadine related compound B IPRS* in the mobile phase.

Chromatographic system
- a stainless steel column 25 cm × 4.6 mm, packed with octadecylsilane bonded to porous silica (4 µm) (Such as J'sphere ODS-M80),
- column temperature: 35°,
- mobile phase: a mixture of 43 volumes of a buffer solution prepared by dissolving 0.865 g of *sodium dodecyl sulphate* in *water*, add 0.5 ml of *trifluoroacetic acid* and dilute to 1000 ml with *water* and 57 volumes of *acetonitrile*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 280 nm,
- injection volume: 100 µl.

Name	Relative retention time	Correction factor
Fluorodesloratadine[1]	0.8	1.67
Desloratadine related compound B[2]	0.9	1.67
Desloratadine	1.0	---

[1]8-Chloro-11-fluoro-11-(piperidin-4-yl)-6,11-dihydro-5*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine,
[2]8-Chloro-11-(1,2,3,6-tetrahydropyridin-4-yl)-6,11-dihydro-5*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine hydrochloride.

Inject reference solution (b) and (c). The test is not valid unless the resolution between the peaks due to desloratadine and desloratadine related compound B is not less than 2.0 in the chromatogram obtained with reference solution (c), the tailing factor is not more than 1.5 and the relative standard deviation for replicate injections is not more than 10.0 per cent in the chromatogram obtained with reference solution (b).

Inject reference solution (b) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to fluorodesloratadine is not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent), the area of any peak corresponding to desloratadine related compound B is not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 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 (b) (0.1 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 with reference solution (b) (0.4 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 (b) (0.05 per cent).

B. Determine by liquid chromatography (2.4.14). *(Use Related substance B, when the impurity profile includes dechloro desloratadine, desloratadine related compound A, or dehydrodesloratadine)*

Buffer solution. Dissolve 1.36 g of *potassium dihydrogen orthophosphate* in *water*, add 10 ml of *triethylamine* and dilute to 1000 ml of *water*, adjusted to pH 2.0 with *dilute orthophosphoric acid*.

Test solution. Dissolve 50 mg of the substance under examination in mobile phase A with the aid of ultrasound and dilute to 100.0 ml with mobile phase A.

Reference solution (a). A 0.005 per cent w/v solution of *desloratadine IPRS* in mobile phase A. Dilute 1.0 ml of the solution to 100.0 ml with mobile phase A.

Reference solution (b). A solution containing 0.01 per cent w/v of *desloratadine IPRS* and 0.000015 per cent w/v *desloratadine related compound A IPRS* in mobile phase A.

Chromatographic system
- a stainless steel column 25 cm × 4.6 mm, packed with octylsilane bonded to porous silica (5 µm) (Such as Hypersil BDS C8),
- column temperature: 35°,
- mobile phase: A. a mixture of 10 volumes of *acetonitrile*, 10 volumes of *methanol* and 80 volumes of the buffer solution,
  B. a mixture of 70 volumes of *acetonitrile*, 5 volumes of *tetrahydrofuran* and 30 volumes of the buffer solution,
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 280 nm,
- injection volume: 60 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	100	0
10	100	0
15	90	10
20	70	30
25	60	40
30	50	50
38	50	50

40	100	0
45	100	0

Name	Relative retention time	Correction factor
Dechloro desloratadine[1]	0.38	1.11
Desloratadine	1.0	---
Desloratadine related compound A[2]	1.30	1.16
Dehydro desloratadine[3]	1.59	---
Loratadine[4]	2.25	1.27

[1]6,11-Dihydro-11-(piperidin-4-ylidene)-5*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine;
[2]8-Bromo-6,11-dihydro-11-(piperidin-4-ylidene)-5*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine;
[3]8-Chloro-11-(piperidin-4-ylidene)benzo[5,6]cyclohepta[1,2-*b*]pyridine;
[4]8-Chloro-6,11-dihydro-11-(1-ethoxycarbonylpiperidin-4-ylidene)-5*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine.

Inject reference solution (a) and (b). The test is not valid unless the resolution between the peaks due to desloratadine and desloratadine related compound A is not less than 3.0 in the chromatogram obtained with reference solution (b), the tailing factor is not more than 3.0 for desloratadine peak and the relative standard deviation for replicate injections is not more than 5.0 per cent in the chromatogram obtained with reference solution (a).

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to dechloro desloratadine, desloratadine related compound A and dehydro desloratadine, each of, is not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1.5 per cent), the area of any peak corresponding to loratadine is not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 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 the areas of all the secondary peaks is not more than 4 times the area of the principal peak in the chromatogram with reference solution (a) (0.4 per cent).

Sulphated ash (2.3.18). Not more than 0.2 per cent, determined on 1.0 g.

Water (2.3.43). Not more than 0.5 per cent, determined by using Method 3.

Assay. Determine by liquid chromatography (2.4.14), as described under Related substances A with the following modifications.

Inject reference solution (a) and (c). The test is not valid unless the resolution between the peaks due to desloratadine and desloratadine related compound B is not less than 2.0 in the chromatogram obtained with reference solution (c), the tailing factor is not more than 1.5 and the relative standard deviation for replicate injections is not more than 1.0 per cent in the chromatogram obtained with reference solution (a).

Inject reference solution (a) and the test solution.

Calculate the content of $C_{19}H_{19}ClN_2$.

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

Labelling. If a test for Related substances other than A is used, then the labeling states with which Related substances test the article complies.

Solubility.

Desloratadine. Freely soluble in *ethanol (95 per cent)*; slightly soluble or very slightly soluble in *heptane*; very slightly soluble or practically insoluble in *water*.