Meclizine Hydrochloride

Published on: 07 February, 2024 **Last date for comments:** 22 March, 2024

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

Description	Details
Document version	1.0
First draft published on IPC website for public comments	February 7, 2024
Last date for comments	**March 22, 2024**
Monograph revisions proposed for inclusion in	**IP 2026**
Tentative effective date of monograph revisions	**July, 2026**
Draft revision published on IPC website for public comments	--
Further follow-up action as required.	

Meclizine Hydrochloride. Page 2830
Change **to**: **Meclizine Hydrochloride**

$C_{25}H_{27}C1N_2$. 2HCl Mol. Wt. 463.9
$C_{25}H_{27}ClN_2$. 2HCl. H_2O Mol.Wt. 481.9

Meclizine Hydrochloride is Piperazine,1-[(4-chlorophenyl)phenylmethyl]-4-[(3-methylphenyl)methyl]-,dihydrochloride, anhydrous or monohydrate;

Meclizine Hydrochloride contains not less than 97.0 per cent and not more than 102.0 per cent of $C_{25}H_{27}C1N_2$,2HCl, calculated on the anhydrous basis.

Category. Antiemetic.

Description. A white or yellowish white, crystalline powder.

Identification

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

B. Dissolve 25 mg in a mixture of 3 ml of *2 M nitric acid* and 5 ml of *ethanol (95 per cent)*. The solution gives reaction (A) of chlorides (2.3.1).

Tests

Related substances

A. Determine by liquid chromatography (2.4.14).

NOTE- On the basis of the synthetic route, perform either Related substances A or *Related substances B is recommended when the isomeclizine impurity may be present.*

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

Reference solution (a). A 0.00025 per cent w/v solution of *meclizine hydrochloride IPRS* in the mobile phase.

Reference solution (*b*). A solution containing 0.001 per cent w/v, each of, *meclizine hydrochloride IPRS* and *4-chlorobenzophenone* in the mobile phase.

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Symmetry shield RP 18),
- mobile phase: dissolve 1.5 g of *1-heptane sulphonic acid sodium salt* in 300 ml of *water,* add 700 ml of *acetonitrile*, adjust to pH 4.0 with *0.05M sulphuric acid*,
- flow rate: 1.3 ml per minute,
- spectrophotometer set at 230 nm,
- injection volume: 20 µl.

Inject reference solution (a) and (b). The test is not valid unless the resolution between the peaks due to meclizine hydrochloride and 4-chlorobenzophenone is not less than 2.0 in the chromatogram obtained with reference solution (b), the column efficiency is not less than 1800 theoretical plates, the tailing factor is not more than 1.5 and the relative standard deviation for replicate injections is not more than 1.5 per cent in the chromatogram obtained with reference solution (a).

Inject reference solution (a) and the test solution. Run the chromatogram 3 times the retention time of principal peak. In the chromatogram obtained with the test solution, the area of any 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 twice the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 per cent).

B. Determine by liquid chromatography (2.4.14).

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

Reference solution (a). A 0.00025 per cent w/v solution of *meclizine hydrochloride IPRS* in the mobile phase.

Reference solution (b). A solution containing 0.00025 per cent w/v, each of, *meclizine hydrochloride IPRS*, *meclizine related compound A IPRS* and *meclizine related compound B IPRS* in the mobile phase.

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as symmetry shield RP 18),
- column temperature: 50°,
- mobile phase: a mixture of 60 volumes of 0.5 per cent w/v solution of *1-heptane sulphonic acid sodium salt* in *water* and 40 volumes of *acetonitrile*, adjust to pH 4.0 with *0.05 M sulphuric acid*,
- flow rate: 2.0 ml per minute,
- spectrophotometer set at 210 nm,
- injection volume: 30 µl.

Name	Relative retention time	Correction factor
3- Methylbenzyl alcohol	0.11	---
1,4- Bis (3- methylbenzyl)piperazine	0.22	1.37
4- Chlorobenzhydrol[1]	0.53	0.77
Meclizine o-chloro isomer[2]	0.81	---
Isomeclizine (meclizine o-methyl isomer)[3]	0.90	0.90
Meclizine	1.0	---

[1]Meclizine related compound A,
[2]1-[2-Chlorophenyl)(phenyl)methyl]-4-(3-methylbenzyl) piperazine,
[3]Meclizine related compound B.

Inject reference solution (a) and (b). The test is not valid unless the resolution between the peaks due to meclizine related compound B and meclizine is not less than 2.0 in the chromatogram obtained with reference solution (b), the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 6.0 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 3-methylbenzyl alcohol, 1,4-bis(3-methylbenzyl) piperazine and meclizine o-chlorobenzhydrol, each of, is not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent), the area of any peak corresponding to 4-chlorobenzhydrol and isomeclizine (meclizine o-methyl isomer), each of, is not more than 0.3 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 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent) and the sum of the areas of all the secondary peaks is not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 per cent). Ignore any peak eluting before 1.7 minutes.

Water (2.3.43). Not more than 1.0 per cent (for anhydrous form) and not more than 5.0 per cent (for monohydrate form), determined on 0.5 g.

Assay. Determine by liquid chromatography (2.4.14).

Test solution. Dissolve 50 mg of the substance under examination in the mobile phase and dilute to 50.0 ml with the mobile phase. Dilute 1.0 ml of the solution to 10.0 ml with the mobile phase.

Reference solution. A 0.01 per cent w/v solution of *meclizine hydrochloride IPRS* in the mobile phase.

Use chromatographic system as described under Related substances A

Inject the reference solution. The test is not valid unless the relative standard deviation for replicate injections is not more than 1.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{25}H_{27}ClN_2,2HCl$.

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

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