Fexofenadine Hydrochloride and Pseudoephedrine Hydrochloride Prolonged-release Tablets

Fexofenadine Hydrochloride and Pseudoephedrine Hydrochloride Sustained-release Tablets; Fexofenadine Hydrochloride and Pseudoephedrine Hydrochloride Extended-release Tablets.

Fexofenadine Hydrochloride and Pseudoephedrine Hydrochloride Prolonged-release Tablets contain not less than 93.0 per cent and not more than 107.0 per cent of the stated amounts of fexofenadine hydrochloride, $C_{32}H_{39}NO_4$.HCl and pseudoephedrine hydrochloride, $C_{10}H_{15}NO$.HCl.

Usual strength. Fexofenadine Hydrochloride, 60 mg and Pseudoephedrine Hydrochloride, 120 mg.

Identification

A. In the Assay, the principal peaks in the chromatogram obtained with test solution (b) correspond to the principal peaks in the chromatogram obtained with reference solution (f).

B. Determine by thin-layer chromatography (2.4.17), coating the plate with silica gel G.

Mobile phase. A mixture of 50 volumes of *toluene*, 45 volumes of *ethanol* and 5 volumes of *ammonium hydroxide*.

Test solution. Transfer a quantity of the powdered tablets containing 30 mg of Fexofenadine Hydrochloride to a 10-ml volumetric flask, add 5.0 ml of *methanol* and shake vigorously for 2 minutes, filter.

Reference solution. Dissolve suitable quantities of *fexofenadine hydrochloride IPRS* and *pseudoephedrine hydrochloride IPRS* in *methanol* to obtain a solution having concentration similar to that of the test solution.

Apply to the plate 10 µl of each solutions. After development, dry the plate in air. Heat the plate at 105° until the odour of ammonia disappears. Allow the plate to cool and examine under ultraviolet light at 254 nm. The Rf value of the principal spots in the chromatogram obtained with the test solution correspond to the spots in the chromatogram obtained with the reference solution.

[*Note*: *The Rf values of fexofenadine and pseudoephedrine are 0.17 and 0.39 respectively]*

Tests

Dissolution (2.5.2). Determine by liquid chromatography (2.4.14).

Apparatus No. 2 (paddle)
Medium. 900 ml of *0.001M hydrochloric acid*,
Speed and time. 50 rpm, 15 minutes and 45 minutes for fexofenadine hydrochloride and 45 minutes, 3 hours, 5 hours and 12 hours for pseudoephedrine hydrochloride.

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 suitable quantities of *fexofenadine hydrochloride IPRS* and *pseudoephedrine hydrochloride IPRS* in the dissolution medium to obtain a solution of known concentration similar to the expected concentration of the test solution.

NOTE: *A small amount of methanol, not more than 0.5 per cent of the total volume, can be used to dissolve fexofenadine hydrochloride IPRS.*

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with sulfonated fluorocarbon polymer coated on a solid spherical core (strong cation- exchange packing) (10 µm) (Such as partisil 10 SCX),
- mobile phase: a mixture of 45 volumes of a buffer solution prepared by dissolving 7.0 g of *monobasic sodium phosphate* in 1000 ml of *water*, adjusted to pH 2.0 with *orthophosphoric acid* and 55 volumes of *acetonitrile*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 210 nm,

– injection volume: 10 µl.

Inject the reference solution. The test is not valid unless the resolution between the peaks due to fexofenadine and pseudoephedrine is not less than 3.0, the tailing factor is not more than 1.5 and the relative standard deviation for replicate injections is not more than 2.0 per cent, for both the peaks.

Inject the reference solution and the test solution.

Calculate the content of $C_{32}H_{39}NO_4$,HCl and $C_{10}H_{15}NO$,HCl in the medium.

Q. After 15 minutes, not less than 65 per cent and at 45 minutes, not less than 80 per cent of the stated amount of $C_{32}H_{39}NO_4$,HCl.

At 45 minutes, not more than 36 per cent, at 3 hours, not less than 45 per cent and not more than 69 per cent, at 5 hours, not less than 61 per cent and not more than 80 per cent and at 12 hours, not less than 80 per cent of the stated amount of $C_{10}H_{15}NO$,HCl.

Related substances. Determine by liquid chromatography (2.4.14),

Buffer solution. A solution prepared by dissolving 6.8 g of *sodium acetate* and 16.22 g of *sodium octanesulphonate* in 1000 ml of *water,* adjusted to pH 4.6 with *glacial acetic acid*.

Solvent mixture. 60 volumes of *methanol* and 40 volumes of the buffer solution.

*Test solution (a).*Disperse a sufficient quantity of the intact tablets containing 0.6 g of Fexofenadine Hydrochloride in 300 ml of *methanol,* with the aid of mechanical shaker for 60 minutes. Add 150 ml of the buffer solution and sonicate for 60 minutes at 40°, with intermittent shaking, cool to room temperature and dilute to 500.0 ml with the buffer solution, filter.

Test solution (b). Dilute 2.0 ml of test solution (a) to 50.0 ml with mobile phase.

Reference solution (a). Weigh and transfer 40 mg of *pseudoephedrine hydrochloride IPRS* to a 50-ml volumetric flask, add 5 ml of *tert-butyl hydroperoxide solution,* sonicate to dissolve. Cover the flask opening with aluminium foil and place the flask in an oven at 90° for 60 minutes, Remove from the oven and allow to cool, dilute to volume with the mobile phase (to generate ephedrine impurity).

Reference solution (b). Dissolve 20 mg, each of, *fexofenadine related compound A IPRS* and decarboxylated degradant in 60 ml of *methanol* and dilute to 100.0 ml with the buffer solution. Dilute 1.0 ml of the solution to 10.0 ml with the mobile phase.

Reference solution (c). A 0.048 per cent w/v solution of *fexofenadine hydrochloride IPRS* in the mobile phase.

Reference solution (d). A 0.12 per cent w/v solution of *pseudoephedrine hydrochloride IPRS* in the mobile phase.

Reference solution (e). Dilute 15.0 ml of reference solution (b), 5.0 ml of reference solution (c) and 4.0 ml of reference solution (d) to 50.0 ml with the mobile phase.

Reference solution (f). Dilute suitable volumes of reference solution (c) and reference solution (d) with the mobile phase to obtain a solution having similar concentration to that of test solution (b).

Chromatographic system

- a stainless steel column 5 cm x 4.6 mm, packed with a sulphonated fluorocarbon polymer coated on spherical core (strong cation exchange packing) (5µm) (Such as Adsorbosphere XL SCX) connected in series to a column 25 cm x 4.6 mm, packed with phenyl group bonded to porous silica (5 µm) (Such as Zorbax SB phenyl),
- column temperature: 35º,
- mobile phase: a mixture of 65 volumes of a buffer solution prepared by dissolving 6.8 g of *sodium acetate* and 16.22 g of *sodium 1-octanesulfonate* in 1000 ml of *water*, adjusted to pH 4.6 with *glacial acetic acid*, and 35 volumes of *methanol*,
- flow rate: 1.5 ml per minute,
- spectrophotometer set 215 nm,
- injection volume: 20 µl.

Name	Relative retention time	Correction factor

Fexofenadine	1.0	---
Pseudoephedrine	1.0	---
Ephedrone[a]	1.2	2.54
Fexofenadine related compound A[1b]	1.2	---
Tertiary dehydrated impurity[2b]	1.8	---
Decarboxylated degradant[3b]	3.1	---

[a]Relative retention time with reference to pseudoephedrine.
[b] Relative retention time with reference to fexofenadine.
[1]2-(4{4-[4-(hydroxydephenyl methyl)piperidin-1-yl]butanoxyl]-2-methyl propanoic acid,
[2]4-[4{4-(Diphenylmethylene)-1-piperidinyl}-1-hydroxybutyl]-2, 2-dimethyl phenyl acetic acid,
[3](±)-4-(1-Hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-butyl]-isopropylbenzene.

Inject reference solution (a) and (e). The test is not valid unless the resolution between the peaks due to pseudoephedrine and ephedrone is not less than 1.7 and the relative standard deviation for replicate injections is not more than 1.0 per cent for pseudoephedrine peak in the chromatogram obtained with reference solution (a), the resolution between the peaks due to fexofenadine and fexofenadine related compound A is not less than 2.0, the relative standard deviation for replicate injections is not more than 1.0 per cent for fexofenadine peak and not more than 3.0 per cent for fexofenadine related compound A and decarboxylated degradant in the chromatogram obtained with reference solution (e).

Inject reference solution (e) and test solution (a). In the chromatogram obtained with test solution (a), the area of any peak corresponding to fexofenadine related compound A is not more than 0.8 times the area of the corresponding peak in the chromatogram obtained with reference solution (e) (0.4 per cent), the area of any peak corresponding to decarboxylated degradant is not more than 0.4 times the area of the corresponding peak in the chromatogram obtained with reference solution (e) (0.2 per cent), the area of any peak corresponding to ephedone is not more than 0.05 times the area of the pseudoephedrine peak in the chromatogram obtained with reference solution (e) (0.2 per cent), the area of any other secondary peak is not more than 0.05 times the area of fexofenadine peak in the chromatogram obtained with reference solution (e) (0.2 per cent). Ignore any peak with an area less than 0.0125 times the area of fexofenadine peak in the chromatogram obtained with reference solution (e) (0.05 per cent).

The sum of all the impurities is not more than 0.8 per cent.

Other tests. Comply with the tests stated under Tablets.

Assay. Determine by liquid chromatography (2.4.14), as described under Related substances.

Inject reference solution (a) and (e). The test is not valid unless the resolution between the peaks due to pseudoephedrine and ephedrone is not less than 1.5 and the relative standard deviation for replicate injections is not more than 1.0 per cent for pseudoephedrine peak in the chromatogram obtained with reference solution (a), the resolution between the peaks due to fexofenadine and fexofenadine related compound A is not less than 2.0 and the relative standard deviation for replicate injection is not more than 1.0 per cent for fexofenadine peak in the chromatogram obtained with reference solution (e).

Inject reference solution (f) and test solution (b).

Calculate the content of $C_{32}H_{39}NO_4.HCl$ and $C_{10}H_{15}NO.HCl$ in the tablets.

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