Rifaximin 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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Rifaximin Tablets

Rifaximin Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of rifaximin, $C_{43}H_{51}N_3O_{11}$.

Usual strengths. 200 mg; 400 mg; 550 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. 2 (Paddle),
Medium. (For 200 mg) 1000 ml of buffer solution prepared by dissolving 12.0 g of *sodium dihydrogen orthophosphate anhydrous* and 0.85 g of *sodium hydroxide* in 800 ml of water, adjusted to pH 7.4 and dilute to 1000 ml with *water*. Add 4.5 g of *sodium lauryl sulphate* and mix,

(For 400 mg and above) 1000 ml of buffer solution prepared by dissolving 12.0 g of *sodium dihydrogen orthophosphate anhydrous* and 0.85 g of *sodium hydroxide* in 800 ml of water, adjusted to pH 7.4 and dilute to 1000 ml with *water*. Add 8 g of *sodium lauryl sulphate* and mix,

Speed and time. 75 rpm, 60 minutes.

Withdraw a suitable volume of the medium and filter. Measure the absorbance of the filtrate, suitably diluted with the dissolution medium if necessary, at the maximum at about 290 nm (2.4.7). Calculate the content of $C_{43}H_{51}N_3O_{11}$, in the medium from the absorbance obtained from 0.002 per cent w/v solution of *rifaximin IPRS* in the dissolution medium.

Q. Not less than 70 per cent of the stated amount of $C_{43}H_{51}N_3O_{11}$.

Related substances. Determine by liquid chromatography (2.4.14).

Test solution. Disperse a quantity of powdered tablets containing 250 mg of Rifaximin in the mobile phase and dilute to 50.0 ml with mobile phase.

Reference solution (a). A 0.0025 percent w/v solution of *rifaximin IPRS*, in the mobile phase.

Reference solution (b). A solution containing 0.0025 per cent w/v of *rifaximin impurity D+H IPRS* and 0.5 per cent w/v of *rifaximin IPRS* in the mobile phase.

Reference solution (c). Dilute 1.0 ml of the reference solution (a) to 5.0 ml with the mobile phase.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with end-capped octadecylsilane bonded to porous silica (5 µm) (Such as Altima C18),
- column temperature: 40º,
- mobile phase: a mixture of 37 volumes of a buffer solution prepared by dissolving 3.16 g of *ammonium formate* in 1000 ml of *water*, adjusted to pH 7.2 with *dilute ammonia* and 63 volumes of a mixture of equal volumes of *acetonitrile* and *methanol*,
- flow rate: 1.4 ml per minute,
- spectrophotometer set at 276 nm,
- injection volume: 20 µl.

Name	Relative retention time
Rifaximin impurities D[1] and H[2]	0.7
Rifaximin (Retention time is about 12 minutes)	1.0

[1] rifaximin Y,

[2](2*S*,16*Z*,18*E*,20*S*,21*S*,22*R*,23*R*,24*R*,25*S*,26*R*,27*S*,28*E*)-5,6,21,23-tetrahydroxy-16-(hydroxymethyl)-27-methoxy-2,4,11,20,22,24,26-heptamethyl-1,15-dioxo-1,2-dihydro2,7-(epoxypentadeca[1,11,13]trienoimino)[1]benzofuro[4,5-*e*]pyrido[1,2-*a*]benzimidazol-25-yl acetate (16-desmethyl-16-(hydroxymethyl)rifaximin).

Inject reference solution (b). The test is not valid unless the resolution between the peaks due to impurity D+H and rifaximin is not less than 3.0.

Inject reference solution (a), (c) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to impurities D and H is not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent), the area of any other secondary peak is not more than twice the area of the principal peak in the chromatogram obtained with reference solution (c) (0.2 per cent) and the sum of the areas of all the secondary peaks is not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1.5 per cent). Ignore any peak with an area less than the area of the principal peak in the chromatogram obtained with reference solution (c) (0.1per cent).

Other tests. Comply with the tests stated under Tablets.

Assay. Determine by liquid chromatography (2.4.14).

Test solution. Weigh and powder 20 tablets. Disperse a quantity of the powder containing 0.5 g of Refiximin in the mobile phase and dilute to 100.0 ml, filter. Dilute 2.0 ml of the filtrate to 250.0 ml with the mobile phase.

Reference solution. A 0.004 per cent w/v solution of *rifaximin IPRS* in the mobile phase.

Use chromatographic system as described under Related substances.

Inject the reference solution and the test solution.

Calculate the content of $C_{43}H_{51}N_3O_{11}$ in the tablets.

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