

Draft Proposal for Comments and Inclusion in The Indian Pharmacopoeia

Rifaximin Tablets

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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
Monograph proposed for inclusion	IP Addendum 2024
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Draft revision published on IPC website for public comments	-
Further follow-up action as required.	

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. 900 ml of buffer solution prepared by dissolving 13.6 g of *sodium acetate* in 800 ml of *water*, add 6 ml of *glacial acetic acid* and dilute to 1000 ml with *water*. Add 2 g of *sodium lauryl sulphate* and mix.

Speed and time. 50 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 0.02 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 μ m) (Such as Altima C18),
- column temperature: 40°,
- 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 μ l.

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-dihydro-2,7-(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 peak of the principal peak in the chromatogram obtained with the reference solution (c) (0.2 per cent) and the sum of 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 principal peak in the chromatogram obtained with reference solution (c) (0.1per cent).

Water (2.3.43). Not more than 8.0 per cent, determined on 0.1 g.

Assay. Determine by liquid chromatography (2.4.14).

Test solution. Weigh and powder 20 tablets. Disperse a quantity of the powdered tablets containing 500 mg 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°.