Nitrofurantoin Oral Suspension

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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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Nitrofurantoin Oral Suspension

Nitrofurantoin Oral Suspension is a suspension of Nitrofurantoin in a suitable aqueous vehicle. It is filled in a sealed container.

Nitrofurantoin Oral Suspension contains not less than 92.0 per cent and not more than 108.0 per cent of the stated amount of nitrofurantoin, $C_8H_6N_4O_5$.

Usual strength. 25 mg per 5 ml.

Identification

A. Mix 10 ml of the oral suspension with 15 ml of *acetone* and heat the solution at 50°, with stirring, to coagulate the excipients, filter. Evaporate the *acetone* with the aid of a warm air blast nearly to dryness, add 10 ml of *acetic acid* and heat to boiling, filter while hot. Cool to room temperature. Filter the precipitated nitrofurantoin, and dry the nitrofurantoin precipitate at 105° for 1 hour. The precipitate complies with the following test.

Determine by infrared absorption spectrophotometry (2.4.6) in mineral oil. Compare the spectrum with that obtained with *nitrofurantoin IPRS* treated in the same manner or with the reference spectrum of nitrofurantoin.

B. 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

pH (2.4.24). 4.5 to 6.5.

Limit of N-(Aminocarbonyl)-N-[([5-Nitro-2-Furanyl] Methylene)-Amino] Glycine. Determine by liquid chromatography (2.4.14).

Test solution. Weigh and transfer a quantity of the oral suspension containing 50 mg of Nitrofurantoin to a 100-ml volumetric flask, add 50 ml of the mobile phase, shake to dissolve and dilute to volume with the mobile phase. Centrifuge a portion of the solution. Dilute 5.0 ml of the supernatant to 50.0 ml with the mobile phase and filter.

Reference solution. A 0.00025 per cent w/v solution of *nitrofurantoin related substances A IPRS* (N-(Aminocarbonyl)-N-[([5-nitro-2-furanyl]-methylene)-amino]-glycine)]in the mobile phase.

Chromatographic system

- a stainless steel column 30 cm x 3.9mm, packed with octadecylsilane bonded to porous silica particles (10 µm),
- mobile phase: a mixture of 88 volumes of a buffer solution prepared by dissolving 6.8 g of *potassium dihydrogen orthophosphate* in 500 ml of *water*, add 30 ml of *1 M sodium hydroxide,* adjusted to pH 7.0 and dilute to 1000 ml with *water* and 12 volumes of *acetonitrile*,
- flow rate: 1.2 ml per minute,
- spectrophotometer set at 375 nm,
- injection volume: 30-60 µl.

NOTE – Adjust the operating parameters so that the nitrofurantoin related compound A peak has a retention time between 3 to 6 minutes.

Inject the reference solution and the test solution. In the chromatogram obtained with the test solution, the height of any peak corresponding to nitrofurantoin related compound A is not more the height of the principal peak in the chromatogram obtained with the reference solution (5.0 per cent).

Other tests. Comply with the tests stated under Oral Liquids.

Assay. Determine by liquid chromatography (2.4.14).

Internal standard solution. A 0.0065 per cent w/v solution of *acetanilide* in the mobile phase.

Test solution. Weigh and transfer a quantity of the oral suspension containing 25 mg of Nitrofurantoin to a 100-ml volumetric flask, add 20 ml of *water* and mix then add 50 ml of *dimethylformamide*, and shake for 20 minutes. Cool to room temperature and dilute to volume with *dimethylformamide.* Centrifuge a portion of the solution. Transfer 4.0 ml of supernatant to a 20-ml volumetric flask, add 15.0ml of the internal standard solution, mix and filter.

Reference solution. Dissolve 25 mg of *nitrofurantoin IPRS* in 50 ml of *dimethylformamide* and 20 ml of *water*. Cool to room temperature and dilute to 100.0 ml with *dimethylformamide.* Transfer 4.0 ml of the solution to a 20-ml volumetric flask, add 15 ml of the internal standard solution and mix.

Chromatographic system

- a stainless steel column 30 cm x 3.9 mm, packed with octadecylsilane bonded to porous silica particles (10 µm),
- mobile phase: a mixture of 88 volumes of a buffer solution prepared by dissolving 6.8 g of *potassium dihydrogen orthophosphate* in 500 ml of *water,* add 30 ml of *1 M sodium hydroxide,* adjusted to pH 7.0 and dilute to 1000 ml with *water*, and 12 volumes of *acetonitrile*,
- flow rate: 1.2 ml per minute,
- spectrophotometer set at 254 nm,
- injection volume: 15 µl.

NOTE – Adjust the operating parameters so that the retention time of the nitrofurantoin peak is about 8 minute and its peak height is about half- full scale.

Inject the reference solution. The test is not valid unless the resolution between the peaks due to acetanilide and nitrofurantoin is not less than 3.5and the relative standard deviation of ratio of peak area of nitrofurantoin to that of peak area of acetanilide (internal standard) for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Determine the weight per ml of the suspension (2.4.29) and calculate the content of $C_8H_6N_4O_5$ weight in volume using ratio of peak area of nitrofurantoin to that of peak area of acetanilide (internal standard).

Storage. Store protected from light and moisture.