Frusemide Oral Solution

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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.

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Frusemide Oral Solution

Furosemide Oral Solution

Frusemide Oral Solution is a solution of frusemide in a suitable vehicle. It may contain a suitable flavoring agent. It is filled in a sealed container.

Frusemide Oral Solution contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of frusemide, $C_{12}H_{11}ClN_2O_5S$.

Usual strengths. 10 mg per ml.

Identification

In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with reference solution (a).

Tests

pH (2.4.24). 7.0 to 10.0.

Limit of Frusemide related compound B. Determine by liquid chromatography (2.4.14).

NOTE —Prepare the solutions immediately before use, Protected from light.

Solvent mixture. 22 volumes of *acetonitrile*, 22 volumes of *water* and 1 volume of *glacial acetic acid.*

Test solution. Dilute a volume of the oral solution containing 100 mg of Frusemide to 100.0 ml with the solvent mixture, filter.

Reference solution (a). A 0.0015 per cent w/v solution of *frusemide related compound B IPRS* (2-amino-4-chloro-5-sulfamoylbenzoic acid) in the solvent mixture.

Reference solution (b). A solution containing 0.01 per cent w/v, each of, *frusemide IPRS* and *frusemide related compound A IPRS* (2-chloro-4-[(furan-2-ylmethyl)amino]-5-sulfamoylbenzoic acid) in the solvent mixture.

Reference solution (c). Dilute 1.0 ml of reference solution (a) to 10.0 ml in the solvent mixture.

Chromatographic system
- a stainless steel column 25 cm × 4.6 mm, packed with nitrile groups bonded to porous silica (5 µm), (Such as Zorbax CN),
- mobile phase: a mixture of 17.5 volumes of *acetonitrile*, 82.5 volumes of *water* and 1 volume of *glacial acetic acid*,
- flow rate: 2 ml per minute,
- spectrophotometer set at 254 nm,
- injection volume: 10 µl.

The relative retention times with reference to furosemide for furosemide related compound A is about 1.1.

Inject reference solution (a), (b) and (c). The test is not valid unless the resolution between the peaks due to frusemide and frusemide related compound A is not less than 1.5 in the chromatogram obtained with reference solution (b), the relative standard deviation for replicate injections is not more than 5.0 per cent in the chromatogram obtained with reference solution (a) and signal-to-noise ratio is not less than 10 in the chromatogram obtained with reference solution (c).

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to frusemide related compound B is not more than the area of principal peak in the chromatogram obtained with reference solution (a) (1.5 per cent).

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

Assay. Determine by liquid chromatography (2.4.14).

[NOTE — Prepare the solutions immediately before use, protected from light.

Solvent mixture. 22 volumes of *acetonitrile*, 22 volumes of *water* and 1 volume of *glacial acetic acid.*

Test solution. Transfer a quantity of the oral solution containing 100 mg of Frusemide into 100-ml volumetric flask, dissolve in 50 ml of the solvent mixture and dilute to volume with the solvent mixture. Filter.

Reference solution (a). A 0.1 per cent w/v solution of *frusemide IPRS* in the solvent mixture.

Reference solution (b). A solution containing 0.01 per cent w/v, each of, *frusemide IPRS* and *frusemide related compound A IPRS* (2-chloro-4-[(furan-2-ylmethyl)amino]-5-sulfamoylbenzoic acid) in the solvent mixture.

Use chromatographic system as described under Limit of Frusemide Related Compound B.

The relative retention times with reference to furosemide for furosemide related compound A is about 1.1.

Inject reference solution (a) and (b). The test is not valid unless the resolution between the peaks due to frusemide and frusemide related compound A is not less than 1.5 in the chromatogram obtained with reference solution (b), the tailing factor is not more than 1.5 and the relative standard deviation for replicate injections is not more than 1.0 per cent in the chromatogram obtained with reference solution (a).

Inject reference solution (a) and the test solution. Run the chromatogram 1.9 times the retention time of the principal peak.

Calculate the content of $C_{12}H_{11}ClN_2O_5S$ in the solution.

Determine the weight per ml of the oral solution (2.4.29) and calculate the content of $C_{12}H_{11}ClN_2O_5S$ weight in volume.

Microbial contamination (2.2.9). Total aerobic viable count is not more than 10^2 CFU per g and total fungal count is not more than10^1 CFU per g determined by plate count. 1 g is free from *Escherichia coli*.

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