Paracetamol and Mefenamic Acid 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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Paracetamol and Mefenamic Acid Suspension

Acetaminophen and Mefenamic Acid Oral Suspension

Paracetamol and Mefenamic Acid Suspension contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of paracetamol, $C_8H_9NO_2$ and mefenamic acid, $C_{15}H_{15}NO_2$.

Usual strengths. Paracetamol 250 mg and Mefenamic Acid 100 mg; Paracetamol 125 mg and Mefenamic Acid 50 mg per 5 ml.

Identification

In the Assay, the principal peaks in the chromatogram obtained with the test solution correspond to the peaks in the chromatogram obtained with the reference solution.

Tests

pH (2.4.24). 4.8 to 5.8.

Related substances. Determine by liquid chromatography (2.4.14).

For Paracetamol— 4-Aminophenol.

NOTE — Prepare the solutions immediately before use.

Buffer solution. Dissolve 8.37 g of *potassium dihydrogen orthophosphate* and 6.71 g of *dipotassium hydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH 6.5 with *dilute orthophosphoric acid* or *dilute sodium hydroxide solution.*

Solvent mixture. ~~Equal volumes of the buffer solution and *acetonitrile.*~~ A mixture of 70 volumes of the buffer solution and 30 volumes of *acetonitrile*.

Test solution. Disperse a quantity of the suspension containing 0.25 g of paracetamol in the solvent mixture, with the aid of ultrasound for 15 minutes and dilute to 100.0 ml with the solvent mixture, filter.

Reference solution (a). A 0.00125 per cent w/v solution of *4-aminophenol IPRS* in the solvent mixture *[Note- If necessary sonicate to dissolve].*

Reference solution (b). A solution containing 0.00125 per cent w/v of *4-aminophenol IPRS*, 0.0025 per cent w/v of *paracetamol IPRS* and 0.001 per cent w/v of *mefenamic acid IPRS* in the solvent mixture *[Note- If necessary sonicate to dissolve].*

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Inertsil ODS 3V),
- mobile phase: A. a mixture of 95 volumes of the buffer solution and 5 volumes of *acetonitrile,*
  B. a mixture of 40 volumes of the buffer solution and 60 volumes of *acetonitrile,*
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 230 nm,
- injection volume: 10 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	100	0
15	100	0
15.5	0	100
25	0	100
28	100	0
32	100	0

Inject reference solution (b) to identify the peaks, due to 4-aminophenol, paracetamol and mefenamic acid.

The elution order is 4-aminophenol, paracetamol and mefenamic acid.

Inject reference solution (a). The test is not valid unless the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 5.0 per cent.

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to 4-aminophenol is not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent).

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

Assay. Determine by liquid chromatography (2.4.14).

Solvent mixture. A 0.04 per cent w/v solution of *sodium hydroxide* in *methanol.*

Test solution. Disperse a suitable quantity of the oral suspension in the solvent mixture (20 per cent of the final volume), with the aid of ultrasound for ~~20~~ 5 minutes with intermittent shaking, add mobile phase (60 per cent of the final volume). Further sonicate for 20 minutes with intermittent shaking and dilute to volume with the mobile phase ~~and dilute with the solvent mixture~~ to obtain a solution having 0.125 per cent w/v of paracetamol and 0.05 per cent w/v of mefenamic acid, filter. Dilute 5.0 ml of the filtrate to 50.0 ml with the mobile phase.

Reference solution. ~~A solution containing 0.125 per cent w/v of *paracetamol IPRS* and 0.05 per cent w/v of *mefenamic acid IPRS* in the solvent mixture.~~ Dissolve 125 mg of *paracetamol IPRS* and 50 mg of *mefenamic acid IPRS* in 20 ml of the solvent mixture with the aid of ultrasound and dilute to 100.0 ml with the mobile phase. Dilute 5.0 ml of the solution to 50.0 ml with the mobile phase.

Chromatographic system

– a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Inertsil ODS 3V),

– mobile phase: a mixture of 50 volumes of a buffer solution prepared by dissolving 8.37 g of *potassium dihydrogen orthophosphate* and 6.71 g of *dipotassium hydrogen orthophosphate* in 1000 ml *water*, adjusted to pH 6.5 with *dilute orthophosphoric acid* or *dilute sodium hydroxide solution*, 40 volumes of *acetonitrile* and 10 volumes of *methanol*,

– flow rate: 1 ml per minute,

– spectrophotometer set at 285 nm,

– injection volume: 10 µl.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent for both peaks.

Inject the reference solution and the test solution.

Determine the weight per ml (2.4.29) of the suspension and calculate the content of $C_8H_9NO_2$ and $C_{15}H_{15}NO_2$ weight in volume.

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