Caffeine Citrate Injection

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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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Caffeine Citrate Injection

Caffeine Citrate Injection is a sterile solution of caffeine citrate, prepared by the interaction of Caffeine and Citric acid monohydrate, in Water for Injections. Sodium citrate may also be present.

Caffeine Citrate Injection contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of caffeine citrate, $C_{14}H_{18}N_4O_9$.

Usual strength. 20 mg per ml.

Description. A clear colourless solution.

Identification

A. 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).

B. It gives reaction (B) of citrates (2.3.1).

Tests

pH (2.4.24). 2.0 to 5.2.

Related substances. Determine by liquid chromatography (2.4.14).

Test solution. Dilute a suitable volume of the injection containing the equivalent of 50 mg of caffeine to 250.0 ml with *water*.

Reference solution (a). A 0.02 per cent w/v solution of *caffeine IPRS* in the *water*.

Reference solution (b). Dilute 1.0 ml of reference solution (a) to 100.0 ml with *water*. Dilute 1.0 ml of the solution to 5.0 ml with *water*.

Reference solution (c). A solution containing 0.02 per cent w/v, each of, *theobromine* (1,7-dimethyl-3,7-dihydro-1H-purine-2,6-dione), *theophylline IPRS* and *caffeine IPRS* in *water*.

Chromatographic system
- a stainless steel column 15 cm x 4.6 mm packed with octadecylsilane bonded to porous silica (5 µm),
- mobile phase: a mixture of 4 volumes of *tetrahydrofuran*, 5 volumes of *acetonitrile* and 191 volumes of *0.01M anhydrous sodium acetate*, previously adjusted to pH 4.5 with *glacial acetic acid*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 275 nm,
- injection volume: 10 µl.

Inject reference solution (c). The test is not valid unless the resolution between the peaks due to theophylline and caffeine is not less than 6.0.

Inject reference solution (b) and the test solution. In the chromatogram obtained with the test solution, the area of any secondary peak is not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent) and the sum of the areas of all the secondary peaks is not more than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent). Ignore any peak with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent).

Other tests. Comply with the tests stated under Parenteral Preparations (Injections).

Assay. Determine by liquid chromatography (2.4.14) as described under Related substances.

Inject reference solution (c). The test is not valid unless the resolution between the peaks due to theophylline and caffeine is not less than 6.0.

Inject reference solution (a) and the test solution.

Calculate the content of $C_{14}H_{18}N_4O_9$ in the injection.

1 mg of $C_8H_{10}N_4O_2$ is equivalent to 1.989 mg of $C_{14}H_{18}N_4O_9$.

Labelling. The label states the strength in terms of the equivalent amount of caffeine.
