Carbamazepine 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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Carbamazepine Oral Suspension

Carbamazepine Oral Suspension is a suspension of Carbamazepine in a suitable vehicle. It may contain suitable flavouring agent. It is filled in a sealed container.

Carbamazepine Oral Suspension contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of carbamazepine, $C_{15}H_{12}N_2O$.

Usual strength. 100 mg per 5 ml.

Identification

A. Transfer a quantity of the oral suspension containing 100 mg of Carbamazepine to a separator containing 20 ml of *0.1M sodium hydroxide* and extract with three successive 20 ml quantities of *methylene chloride*. Dry the combined extracts over *anhydrous sodium sulphate* and evaporate to dryness. The residue complies with the following test.

Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *carbamazepine IPRS* or with the reference spectrum of carbamazepine.

B. 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

Related substances. Determine by liquid chromatography (2.4.14).

Test solution. Weigh and transfer a quantity of the oral suspension containing 50mg of Carbamazepine to a 50-ml volumetric flask, add 35 ml of *methanol*, shake by mechanical means for 30 minutes and sonicate for 2 minutes, dilute to volume with *methanol* and shake for 5 minutes and filter.

Reference solution. A solution containing 0.0002 per cent w/v, each of, *carbamazepine IPRS, carbamazepine related compound A IPRS* (10,11-Dihydrocarbamazepine) and *carbamazepine related compound B IPRS* (5*H*-Dibenz[b,f]azepine in *methanol.*

Chromatographic system

- a stainless steel column 10 cm x 2.1 mm, packed with nitrile group bonded to porous silica (1.8 µm) (Such as Nucleosil CN),
- column temperature: 40°,
- mobile phase: A. a buffer solution prepared by mixing 0.5 ml of *triethylamine* and 0.5 ml of *formic acid* to 1000 ml of *water*,
  B. a 0.025 per cent of *formic acid* in *methanol*,
- a gradient programme using the conditions given below,
- flow rate: 0.3 ml per minute,
- spectrophotometer set at 230 nm,
- injection volume: 2 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	80	20
3	80	20
12	60	40
18	45	55
20	45	55
20.1	80	20
23	80	20

Name	Relative retention time
Carbamazepine related compound A[1*]	0.96
Carbamazepine	1.0
Carbamazepine related compound B[2]	1.45

[*]Process impurity included for identification only, controlled in the drug substance, and are not to be reported or included in the total degradation product.

[1]10,11-Dihydrocarbamazepine,
[2]5H-Dibenz[b,f]azepine.

Inject the reference solution. The test is not valid unless the resolution between the peaks due to carbamazepine related compound A and carbamazepine is not less than 1.7, and the relative standard deviation for replicate injections is not more than 2.0 per cent for each peak.

Inject the reference solution and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to carbamazepine related compound B is not more than the area of the corresponding peak in the chromatogram obtained with the reference solution (0.2 per cent), the area of any other secondary peak is not more than the area of the principal peak in the chromatogram obtained with the reference solution (0.2 per cent), and the sum of areas of all the secondary peaks is not more than 2.5 times the area of the principal peak in the chromatogram obtained with the reference solution (0.5 per cent). Ignore any peak with an area less than 0.25 times the area of the principal peak in the chromatogram obtained with the reference solution (0.05 percent).

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

Assay. Determine by liquid chromatography (2.4.14) as described under Related substances with the following modifications.

Test solution. Weigh and transfer a quantity of the oral suspension containing 20 mg of Carbamazepine to a 200-ml volumetric flask, add 140 ml of *methanol*, shake by mechanical means for 30 minutes and sonicate for 2 minutes, dilute to volume with *methanol*, filter.

Reference solution (a). A 0.01 per cent w/v solution of *carbamazepine IPRS* in *methanol*.

Reference solution (b). A solution containing 0.0002 per cent w/v, each of, *carbamazepine IPRS* and *carbamazepine related compound A IPRS* (10,11-Dihydrocarbamazepine) in *methanol*.

Inject reference solution (a) and (b). The test is not valid unless the resolution between the peaks due to carbamazepine related compound A and carbamazepine is not less than 1.7 in the chromatogram obtained with reference solution (b), the tailing factor is not more than 2.0 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.

Determine the weight per ml of the suspension (2.4.29) and calculate the content of $C_{15}H_{12}N_2O$ weight in volume.

Microbial contamination (2.2.9). Total microbial count is not more than 10^2 CFU per g. 10 g is free from *Salmonella species* and 1 g is free from *Escherichia coli*.

Storage. Store protected from light. Do not freeze and prevent exposure to excessive heat.