Phenytoin

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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

Description	Details
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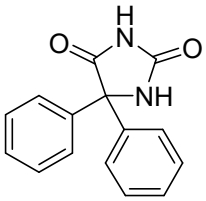
Further follow-up action as required.	

Phenytoin. Page 3262
Change **to: Phenytoin**
Diphenylhydantoin



$C_{15}H_{12}N_2O_2$ Mol. Wt. 252.3

Phenytoin is 2,4-imidazolidinedione, 5,5 diphenyl.

Phenytoin contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{15}H_{12}N_2O_2$, calculated on the dried basis.

Category. Anticonvulsant.

Description. A white or almost white, crystalline powder.

Identification

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

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

Tests

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. Equal volumes of *water* and mobile phase B.

Test solution. Dissolve 50 mg of the substance under examination in the solvent mixture and dilute to 50.0 ml with the solvent mixture.

Reference solution. A solution containing 0.0001 per cent w/v of *phenytoin IPRS,* 0.0005 per cent w/v of *phenytoin related compound A IPRS,* 0.0009 per cent w/v of *phenytoin related compound B IPRS* and 0.0001 per cent w/v of *benzophenone IPRS* in the solvent mixture.

Chromatographic system
- -a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (3 µm) (Such as Inertsil ODS-3),
- -mobile phase: A. a *0.05 M potassium dihydrogen phosphate solution*, adjusted to pH 2.5 with *orthophosphoric acid*,
  B. a mixture of 40 volumes of *acetonitrile* and 60 volumes of *methanol,*
- -a gradient programme using the conditions given below,
- -flow rate: 1 ml per minute,
- -spectrophotometer set at 220 nm,
- -injection volume: 20 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)

0	60	40
23	60	40
38	42	58
45	30	70
50	30	70
51	60	40
55	60	40

Name	Relative retention time
Phenytoin related compound A[1]	0.14
Phenytoin related compound B[2]	0.53
Phenytoin	1.0
Benzophenone[3]	2.11
Benzil	2.23

[1]2,2-Diphenylglycine,
[2] 2,2-Diphenyl-2-ureidoacetic acid,
[3]Diphenylmethanone.

Inject the reference solution. The test is not valid unless the relative standard deviation for replicate injections is not more than 5.0 per cent for phenytoin peak and the signal-to-noise ratio is not less than 10.0.

Inject the reference solution and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to phenytoin related compound A is not more than the area of the corresponding peak in the chromatogram obtained with the reference solution (0.5 per cent), the area of any peak corresponding to phenytoin related compound B is not more than the area of the corresponding peak in the chromatogram obtained with the reference solution (0.9 per cent), the area of any peak corresponding to benzophenone is not more than the area of the corresponding peak in the chromatogram obtained with the reference solution (0.1 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 (0.1 per cent) and the sum of the areas of all the secondary peaks other than benzophenone is not more than 9 times the area of the principal peak in the chromatogram obtained with the reference solution (0.9 per cent). Ignore any peak with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with the reference solution (0.05 per cent).

Heavy metals (2.3.13). 2.0 g complies with the limit test for heavy metals, Method B (10 ppm).

Loss on drying (2.4.19). Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, for 4 hours.

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

Test solution. Dissolve 20 mg of the substance under examination in the solvent mixture and dilute to 100.0 ml with the solvent mixture.

Reference solution. A 0.02 per cent w/v solution of *phenytoin IPRS* in the solvent mixture.

Inject the reference solution. The test is not valid unless 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.

Inject the reference solution and the test solution.

Calculate the content of $C_{15}H_{12}N_2O_2$.

Storage. Store protected from moisture.