Phenytoin Sodium

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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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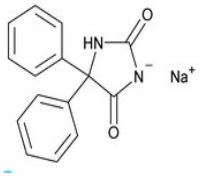
Further follow-up action as required.	

Phenytoin Sodium. Page 3263
Change **to: Phenytoin Sodium**
Diphenylhydantoin Sodium



$C_{15}H_{11}N_2NaO_2$ Mol. Wt. 274.3

Phenytoin Sodium is 2,4-imidazolidinedione, 5,5 diphenyl, monosodium salt.

Phenytoin Sodium contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{15}H_{11}N_2NaO_2$, calculated on the dried basis.

Category. Anticonvulsant; antiarrhythmic.

Description. A white powder; somewhat hygroscopic and on exposure to air gradually absorbs carbon dioxide.

Identification

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

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

C. Incinerate 0.1 g; the residue after neutralisation with *hydrochloric acid* and addition of 2 ml of *water* gives the reactions of sodium salts (2.3.1).

Tests

Related substances. Determine by liquid chromatography (2.4.14).

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

Reference solution (a). A solution containing 0.00005 per cent w/v of *benzophenone IPRS,* 0.0001 per cent w/v of *phenytoin IPRS* and 0.0009 per cent w/v, each of, *phenytoin related compound A IPRS* and *phenytoin related compound B IPRS* in the mobile phase.

Reference solution (b). A solution containing 0.01 per cent w/v of *phenytoin IPRS* and 0.015 per cent w/v of *benzoin* in 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 Zorbax ODS),
-mobile phase: a mixture of 45 volumes of *0.05 M ammonium dihydrogen phosphate*, adjusted to pH 2.5 with *orthophosphoric acid*, 35 volumes of *acetonitrile* and 20 volumes of *methanol,*
-flow rate: 1.5 ml per minute,
-spectrophotometer set at 220 nm,
-injection volume: 20 µl.

Name	Relative retention time
Phenytoin related compound A[1]	0.5
Phenytoin related compound B[2]	0.6
Phenytoin	1.0
Benzophenone[3]	2.9

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

The relative retention time with reference to phenytoin, for benzoin is about 1.3.

Inject reference solution (a) and (b). The test is not valid unless the resolution between the peaks due to phenytoin and benzoin is not less than 1.5 in the chromatogram obtained with reference solution (b) and the relative standard deviation for replicate injections is not more than 5.0 per cent for each component in the chromatogram obtained with reference solution (a).

Inject reference solution (a) 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 0.56 times the area of the corresponding peak in the chromatogram obtained with reference solution (a) (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 reference solution (a) (0.9 per cent), the area of any peak corresponding to benzophenone is not more than twice the area of the corresponding peak in the chromatogram obtained with reference solution (a) (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 reference solution (a) (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 reference solution (a) (0.9 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 2.5 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).

Test solution. Dissolve 50 mg of the substance under examination in the mobile phase and dilute to 100.0 ml with the mobile phase. Dilute 1.0 ml of the solution to 10.0 ml with the mobile phase.

Reference solution (a). A 0.005 per cent w/v solution of *phenytoin IPRS* in the mobile phase.

Reference solution (b). A solution containing 0.01 per cent w/v of *phenytoin IPRS* and 0.015 per cent w/v of *benzoin* in the mobile phase.

Use the chromatographic system as described under Related substances.

The relative retention time with reference to phenytoin, for benzoin is about 1.3.

Inject reference solution (a) and (b). The test is not valid unless the resolution between the peaks due to phenytoin and benzoin 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.

Calculate the content of $C_{15}H_{11}N_2NaO_2$.
Storage. Store protected from moisture.