Pantoprazole for Injection

Published on: 19 December, 2022 **Last date for comments:** 17 February, 2023

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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
Document version	1.0
Monograph proposed for inclusion	IP Addendum 2024
Tentative effective date of monograph	July, 2024
First draft published on IPC website for public comments	19 December, 2022
Draft revision published on IPC website for public comments	-
Further follow-up action as required.	

Pantoprazole for Injection

Pantoprazole Sodium for Injection

Pantoprazole for Injection is a sterile material consisting of Pantoprazole Sodium Sesquihydrate with or without excipients. It is supplied in a sealed container

The injection is constituted by dissolving the contents of the sealed container in the requisite amount of sterile Water for Injections, immediately before use.

The contents of the sealed container comply with the requirements for Powders for Injections or Infusions stated under Parenteral Preparations and with the following requirements.

Pantoprazole Injection contains Pantoprazole Sodium equivalent to not less than 93.0 per cent and not more than 105.0 per cent of the stated amount of pantoprazole, $C_{16}H_{15}F_2N_3O_4S$.

Usual strengths. 40 mg.

Identification

A. Shake a quantity of powder containing 40 mg of Pantoprazole with 10 ml of *acetone* and filter. Evaporate to dryness. Dry the residue at 60° for 30 minutes. On the residue determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *pantoprazole sodium IPRS* or with the reference spectrum of pantoprazole sodium.

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).

C. It gives the reactions of sodium salts (2.3.1).

Tests

Appearance of solution. A solution containing the equivalent of 0.4 per cent w/v of pantoprazole is clear (2.4.1) and not more intensely colored than reference solution BS5 or BYS5 (2.4.1).

Acidity or alkalinity. pH (2.4.24) 9.0 to 11.5, determined in a solution containing the equivalent of 0.4 per cent w/v solution of pantoprazole.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. Equal volumes of *acetonitrile* and *0.001 M sodium hydroxide.*

Test solution. Shake a quantity of powder containing equivalent of 40 mg of Pantoprazole in the solvent mixture and dilute to 100.0 ml with the solvent mixture.

Reference solution (a). A solution of *pantoprazole sodium IPRS* in the solvent mixture containing the equivalent of 0.0002 per cent w/v solution of pantoprazole.

Reference solution (b). A solution containing 0.04 per cent w/v of *pantoprazole IPRS* and 0.0006 per cent w/v of *pantoprazole related compound D+ F IPRS* in the solvent mixture.

Reference solution (c). Dilute 2.0 ml of reference solution (a) to 10.0 ml with solvent mixture.

Chromatographic system

- a stainless steel column 12.5 cm x 4.0 mm packed with octadecylsilane bonded to porous silica (5µm), (Such as Hypersil ODS),
- column temperature: 40º,

−sample temperature: 5º,
− mobile phase: A. *0.01M dipotassium hydrogen phosphate trihydrate* adjusted to pH 7.0 with 20 per cent v/v solution of *orthophosphoric acid*,
B. a mixture of 1 volumes of *water* and 99 volumes of *acetonitrile*,
−a gradient programme using the conditions given below,
−flow rate: 1 ml per minute,
−spectrophotometer set at 290 nm,
−injection volume: 20 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	90	10
3	90	10
33	60	40
48	15	85
50	90	10
60	90	10

Name	Relative retention time	Correction factor
Pantoprazole Related Compound C[1]	0.6	0.6
Pantoprazole Related Compound A[2]	0.9	---
Pantoprazole (Retention time; about 22 minutes)	1.0	---
Pantoprazole Related Compound D[3] and F[4]	1.1	---
Pantoprazole Related Compound E[5]	1.3	---
Pantoprazole Related Compound B[6]	1.4	---

[1]5-(difluoromethoxy)-1*H*-benzimidazole-2-thiol
[2]5-(Difluoromethoxy)-2-[[(3,4- dimethoxypyridin - 2-yl) methyl] sulfonyl]-1*H*- benzimidazole,
[3]5-(Difluoromethoxy)-2-[(RS)-[(3, 4-dimethoxypyridin-2-yl)methyl] sulfinyl]-1-methyl-1*H*- benzimidazole,
[4]6-(Difluoromethoxy)-2-[(RS)-[(3, 4-dimethoxypyridin-2-yl)methyl] sulfinyl]-1-methyl-1*H*- benzimidazole,
[5]mixture of the stereoisomers of 6,6'-bis(difluoromethoxy)-2,2'-bis[[(3,4-dimethoxypyridin-2yl)methyl]-1*H*,1'*H*-5,5'-bibenzimidazoly,
[6]5-(Difluoromethoxy)-2-[[(3,4- dimethoxypyridin --2-yl)methyl] sulfinyl]-1*H* benzimidazole.
* *Related compound D and F are not fully resolved and should be integrated together.*

Inject reference solutions (b). The test is not valid unless the resolution between the peaks due to pantoprazole related compound D and F (D+F) and pantoprazole is not less than 3.0.

Inject reference solution (a), (c) and the test solution. In the chromatogram obtained with the test solution, the sum of the areas of pantoprazole related Compound D and F is not more than 3 times the area of principal peak in the chromatogram obtained with reference solution (a) (1.5 per cent), the area of any peak corresponding to pantoprazole related compound A is not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent), the area of any other secondary peak is not more than 0.4 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent) and the sum of areas of all the secondary peaks is not more than 4 time the area of the principal peak in the chromatogram obtained with reference solution (a) (2.0 per cent). Ignore any peak with an area less than the area of the principal peak in the chromatogram obtained with reference solution (c) (0.1 per cent).

Other tests. Comply with the tests stated under Parenteral Preparations (Powder for Injection).

Assay. Determine by liquid chromatography (2.4.14).

Solvent mixture. Equal volumes of *acetonitrile* and *0.001 M sodium hydroxide.*

Test solution. Reconstitute 1 vial with requisite volume of water for injection, shake. Reconstitute 9 more vials. Pool the content of 10 vials to prepare a composite sample. Dilute a sutable volume of pooled sample with the solvent mixture to obtain a solution containing 0.004 per cent w/v of Pantoprazole.

Reference solution (a). A 0.0045 per cent w/v solution of *pantoprazole sodium IPRS* in the solvent mixture.

Reference solution (b). A solution containing 0.045 per cent w/v of *pantoprazole sodium IPRS* and 0.0005 per cent w/v of *pantoprazole related compound A IPRS* in the solvent mixture

Chromatographic system

- a stainless steel column 12.5 cm x 4.0 mm packed with octadecylsilane bonded to porous silica (5µm), (Such as Hypersil ODS),
- sample temperature: 5º,
- mobile phase: a mixture of 65 volumes of *0.01M dipotassium hydrogen phosphate trihydrate* adjusted to pH 7.0 with 20 per cent v/v solution of *orthophosphoric acid* and 35 volumes of *acetonitrile.*
- flow rate: 1 ml per minute,
- spectrophotometer set at 290 nm,
- injection volume: 20 µl.

Inject reference solutions (b). The test is not valid unless the resolution between the peaks due to pantoprazole related compound A and pantoprazole is not less than 1.5.

Inject reference solution (a) and the test solution.

Calculate the content of $C_{16}H_{15}F_2N_3O_4S$ in the injection.

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

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