ANALYTICAL METHOD VALIDATION COMMITTEE FOR NON PHARMACOPOEIAL PRODUCT

DEPARTMENT OF DRUG ADMINISTRATION

Pantoprazole Powder for Injection

S.N	**Test Parameter**	**Limit**
1.	Identification	Positive for Pantoprazole
2.	Uniformity of weight	As per IP (latest edition)
3.	pH	9.0 to 12.0
4.	Clarity of the solution	Must be clear, leaving no visible residue as undissolved matter.
5.	Water Content	Not more than 5%
6.	Particulate matter	≥ 10 µm: NMT 6000 Particles/container ≤ 25 µm: NMT 6000 Particles/container
7.	Bacterial Endotoxin test	Not more than 0.125 EU/mg of Pantoprazole
8.	Sterility (Membrane filtration)	Shows no growth of microorganisms.
9.	Assay	90 % to 110 % of the stated amount (36 mg to 44 mg of the stated amount)

1. Identification:

1.1 Pantoprazole:

In the assay, the principle peak in the chromatogram obtained with the sample solution should correspond to the peak in the chromatogram obtained with the reference standard solution of Pantoprazole.

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2. pH

Calibrate the pH meter before use. Constitute 25 vials each with 2 ml of carbon dioxide free water and withdraw all contents with the help of hypodermic needle syringe. Mix and take the solution in a rinsed clean beaker of about 100 ml capacity, immerse the electrode of pre calibrated pH meter and take the reading when the reading on the screen is constant.

3. Water content

Determine the water content on 0.1 g of sample in dried methanol in the titration vessel. Calculate the water content (WC) using the following formula:

$$WC\ in\ \% \frac{w}{w} = \frac{K.F.Reading\ X\ Average\ K.F\ factor}{Wt\ of\ sample\ in\ mg} X\ 100$$

4. Clarity of the solution

Constitute the cake in the vial with the labeled amount of Sodium chloride injection IP 0.9 % w/v with the help of a hypodermic needle syringe. The solid dissolves completely, leaving no residue as undissolved matter. The constituted solution is not significantly less clear than an equal volume of diluents or Purified water contained in similar vessel and examined similiarly. The solution is essentially free from foreign matter that can be observed on visual inspection.

5. Particulate matter (By Light Obscuration Particle Counter)

As per Indian Pharmacopoeia (latest edition)

6. Bacterial Endotoxin Test

As per Indian Pharmacopoeia (latest edition)

7. Sterility test

As per Indian Pharmacopoeia (latest edition)

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8. Assay:

8.1 Reagents Required:

1. Acetonitrile (HPLC Grade)
2. Water (HPLC Grade)
3. Methanol (HPLC Grade)
4. Dibasic ammonium phosphate
5. Orthophosphoric acid

8.2 Preparation of reagent solution:

8.2.1 Solvent mixture: A mixture of Acetonitrile and water (1:1)

8.2.2 Buffer: Dissolve 1.32 g of dibasic ammonium phosphate in 1000 ml of water; adjust pH to 7.5 with orthophosphoric acid.

8.2.3 Mobile phase: A mixture of Buffer:Acetonitrile and Methanol in the ratio of 47:40:14, pass through a membrane filter having a 0.45 µm or finer porosity.

8.3 Chromatographic system

Column: Octadecylsilane (C18), (250*4.6 mm), 5 µm

Flow rate: 1.0 ml/min

Detector: UV Detector

Wavelength: 285 nm

Injection volume: 20 µl

Oven temperature: Ambient

8.4 Standard Solution:

Weigh accurately about 40 mg of working standard of Pantoprazole and transfer into 50 ml volumetric flask. Dissolve with solvent mixture and make up the volume to 50 ml with solvent mixture. Dilute 2 ml of the resulting solution to 25 ml with mobile phase. Filter the resulting solution through 0.2 µm membrane filter paper. Use the solution immediately.

8.5 Sample Preparation:

Weigh twenty units taken randomly, and record their fill weight. Empty the content of the entire ten containers and mix all the content and keep the content in the air tight container. Weigh accurately about the sample equivalent to 40 mg of pantoprazole and transfer into 50 ml volumetric flask. Dissolve with diluents and make up the volume to 50 ml with solvent mixture. Dilute 2 ml of the resulting solution to 25 ml with mobile phase. Filter the resulting solution through 0.2 µm membrane filter paper. Use the solution immediately.

8.6 Chromatographic Procedure:

Inject 20 µl of standard and sample solution separately and obtain the respective chromatogram. Measure the peak responses.

8.7 System suitability:

Inject 20 µl of standard solution of Pantoprazole as per above mentioned chromatographic condition. In the chromatogram obtained from the standard preparation, the column efficiency determined from the major peak should not be less than 2000 theoretical plates, the tailing factor should be not more than 2.0 and the relative standard deviation of replicate injections should not more be than 2.0 %. Inject 20µl of the sample preparation and chromatograph as per above mentioned chromatographic condition. Calculate the result from the formula given below.

2.8 Calculations:

Content of:

$$\frac{\textbf{Spl Peak Area}}{\textbf{Std Peak Area}} \textbf{ X } \frac{\textbf{Std wt}}{\textbf{Std Dil.}} \textbf{ X } \frac{\textbf{Spl Dil.}}{\textbf{Spl wt}} \textbf{ X Average wt X Std Potency } (\%) \textbf{X} \frac{(\textbf{100} - \textbf{Std LOD})}{\textbf{100}} \textbf{X } \frac{\textbf{M.W. of Pantoprazole}}{\textbf{M.W. of Pantoprazole Sodium}}$$