THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR PZOLENOV (PANTOPRAZOLE (AS SODIUM SESQUIHYDRATE) 40 MG) POWDER FOR SOLUTION FOR INJECTION+ STERILE SODIUM CHLORIDE 0.9% W/V DILUENT

Version number 1.0
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1. Introduction

PZOLENOV powder for solution for injection is a generic medicinal product containing the active substance pantoprazole sodium sesquihydrate. The reference product is 'Pantozol 40 mg powder for solution for injection (Altana Pharma)'. Pantoprazole is a substituted benzimidazole which inhibits the secretion of hydrochloric acid in the stomach by specific action on the proton pumps of the parietal cells (a gastric proton pump inhibitor, (PPI). Pantoprazole is converted to its active form in the acidic environment in the parietal cells where it inhibits the H+, K+ ATPase enzyme, i.e., the final stage in the production of hydrochloric acid in the stomach. The inhibition is dose-dependent and affects both basal and stimulated acid secretion. As other proton pump inhibitors and H2 receptor inhibitors, treatment with pantoprazole causes a reduced acidity in the stomach and thereby an increase in gastrin in proportion to the reduction in acidity. The increase in gastrin is reversible. Since pantoprazole binds to the enzyme distal to the cell receptor level, the substance can affect hydrochloric acid secretion independently of stimulation by other substances (acetylcholine, histamine, gastrin). The effect is the same whether the product is given orally or intravenously. PZOLENOV powder for solution for injection is approved in Tanzania for use in adults only.

Product details

Registration number	TAN 23 HM 0280
Brand name	PZOLENOV
Generic name, strength, and form	Each vial contains: Pantoprazole Sodium equivalent to Pantoprazole 40mg Diluent: Sodium Chloride Injection 0.9% w/v
ATC classification	A02BC02 Proton pump inhibitors
Distribution category	POM
Country of origin	India
Associated product	N/A
Marketing Authorization Holder	Advanov Pharma Pvt. Ltd. A-202, Empire Business Hub, Science city road, Ahmedabad-380060, Gujarat, India.
Local Technical Representative	Global Dar Es Salaam Pharmacy Ltd, P.O. BOX 21562, Dar es Salaam,

1.1 Assessment procedure

The application for registration of PZOLENOV powder for solution for injection was submitted on 25/08/2022. The product underwent full assessment. Assessment was completed in 3 (three) rounds of evaluation and the product was registered on 01/06/2023.

1.2 Information for users

Visual description of the finished product	White to off white powder
Primary packing material	Amber glass vial USP type III
Secondary packing materials	Printed carton box
Shelf-life and storage condition	24 Months, Do not store above 30°C, Protect from light. Do not freeze. 12 hours when stored at 2-80C. (after after reconstitution or dilution)
Route of administration	Intravenous
Therapeutic indications	Pantoprazole Injection is Indicated for 1. Reflux Esophagitis 2. Gastric and duodenal ulcer 3. Zollinger-Ellison-Syndrome and other pathological hyper secretory conditions

2. Labelling and product information

Summary of product characteristics
The SmPC included all the relevant information to ensure correct and safe use of the medicine by healthcare providers. The complete SmPC can be accessed here.

Package insert/leaflet
The package insert is confirmed to be derived from the SmPC and contains sufficient data for the end user. Since the product is POM, the package insert contains full prescribing information as per SmPC.

Container labels
The product label information is presented in English. Details in the secondary pack label include:

Brand name: PZOLENOV

Composition: Each vial contains: Pantoprazole Sodium equivalent to Pantoprazole 40mg

Pack size: 1 Vial + 1 Ampoule

Manufacturing details: batch number, manufacturing date, and expiry date

Storage conditions: Do not store above 30 ^{o}C. Protect from light. Do not freeze. The reconstituted solution to be used immediately. If not used can be stored upto12 hours at 2°C to 8°C at aseptic condition. Discard the unused content

Manufacturer address: Physical address of release site

Unique identifier: Not applicable

Special warnings/precautions or instructions for use: Reconstitution details:- A ready-to-use solution is prepared by injecting 10 ml of sodium chloride 9 mg/ml (0.9%) solution for injection into the vial containing the dry powder. Shake to dissolve.

If foreign particle is visible in the vial after dissolving the contents, do not use the solution

The details of the primary pack include:

Brand name and strength: PZOLENOV

Manufacturing details: batch number, manufacturing date and expiry date

Name of manufacturer: Ratnamani Healthcare Pvt. Ltd

The content of the primary and secondary labels was aligned to the requirements of the Part V of the Compendium: Guidelines on Format and Content of Product Labels for Medicinal products. The label contains sufficient information for proper identification of the medicine and post marketing follow up of the product.

Mock labels are appended as annex I.

3. Scientific discussion

Quality of Active Pharmaceutical Ingredient

Information on quality of the API was submitted in form of Full details.

A. Pantoprazole Sodium Sesquihydrate from Vasudha Pharma Chem Limited

General Information

Pantoprazole Sodium Sesquihydrate API is compendia in Ph.Eur., BP, USP.

Molecular formula: $C_{16}H_{14}F_2N_3NaO_4S$, 1½ H_2O

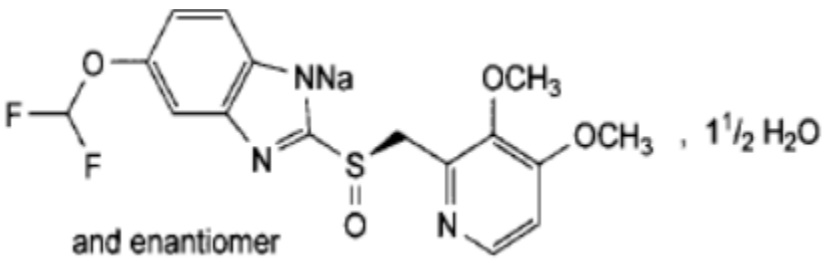
Chemical name:

1H-Benzimidazole, 5-(difluoromethoxy)-2-[[(3, 4- dimethoxy-2-pyridyl) methyl] sulfinyl]-, sodium salt, hydrate (2:3)

5-(difluoromethoxy)-2-[[(3, 4-dimethoxy-2- pyridyl) methyl] sulfinyl] benzimidazole, sodium salt, sesquihydrate

Sodium 5-(difluoromethoxy)-2-[(RS)-[(3, 4- dimethoxypyridin-2-yl) methyl] sulfinyl] benzimidazol-1-ide sesquihydrate.

Structure:



General properties

Pantoprazole Sodium is a white or almost white powder, freely soluble in water and in ethanol (96 percent), practically insoluble in hexane. Pantoprazole Sodium Sesquihydrate molecule exhibits polymorphism and is form- I. Nevertheless, as active is present in the drug product dissolved in water, hence the polymorphic form and particle size distribution are not considered as critical quality aspects.

Manufacture

Pantoprazole Sodium API manufacturers are Vasudha Pharma Chem Limited, Unit-II, Plot No. 79, Jawaharlal Nehru Pharma City, Parawada, Visakhapatnam - 531019, Andhra Pradesh, INDIA and Rajasthan Antibiotics Limited, A-619 & 630, RIICO Industrial Area, Bhiwadi – 301 019, District - Alwar, Rajasthan, INDIA. The manufacturing complies with GMP requirements as evidenced by the GMP certificates issued. Pantoprazole Sodium API is manufactured by chemical synthesis using conventional techniques. Sufficient controls of quality of materials and in-process checks were employed throughout the manufacturing process.

Specifications

The API specifications were set as per Ph. Eur standards and ICHQ3A. The parameters monitored during quality control are: Appearance, solubility, identification, appearance of solution, optical rotation, water, assay, related substances, residual solvents, and bacterial endotoxins. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

Vasudha Pharma Chem Limited:

The re-test period of Pantoprazole Sodium API is 48 months when packed in food grade double polythene bags (Inner transparent and outer black) which is then packed in HDPE drums with storage condition ‘Store below 25°C’.

Rajasthan Antibiotics Limited:

The re-test period of Pantoprazole Sodium API is 36 months when packed in Aluminum Container Rubber stopper with Aluminum Seal with storage condition ‘Store below 30°C’.

Quality of the Finished Pharmaceutical Product

Formulation

PZOLENOV powder for solution for injection is a white to off white powder

PZOLENOV powder for solution for injection contains only Pantoprazole Sodium.

Diluent:
Sodium Chloride Injection BP 0.9% w/v contains only Sodium Chloride and Water for Injection.

Manufacture

Pzolenov (Pantoprazole for Injection 40 mg):

The finished product manufacturer is Ratnamani Healthcare Pvt. Ltd., Survey No.: 750/1, Ahmedabad-Mehsana Highway,Vill: Indrad-382721, Tal. Kadi,Dist.: Mehsana, Gujarat. India. The compliance of the sites to TMDA GMP standards was confirmed through site inspection on DD/MM/YYYY.

Sodium Chloride Injection 0.9% w/v:

The finished product manufacturer is Amanta Healthcare Ltd., Plot no.: 876, N.H. No.: 8, Vill. Hariyala, Dist - Kheda - 387411, Gujarat, India. The compliance of the sites to TMDA GMP standards was confirmed through site inspection on DD/MM/YYYY.

Specifications

Pzolenov (Pantoprazole for Injection 40 mg):

The FPP is compendia. The manufacturer controls the quality of the finished product as per in-house standards and ICH requirements. The parameters monitored during quality control are: Description, Identification by HPLC and IR, Identification by test of Sodium, Average filled weight, Uniformity of weight, pH, Water (By KF), Particulate matter, Assay, Related compounds, Sterility, and Bacteria endotoxins. Compliance to the standard was established using batch analysis data and stability data.

Sodium Chloride Injection BP 0.9% w/v:

The FPP is compendia. The manufacturer controls the quality of the finished product as per BP standards and ICH requirements. The parameters monitored during quality control are: Appearance, Identification by test of sodium salt, identification by test of chlorides, extractable

volume (ml) assay of sodiumchloride, pH, bacteria endotoxins, particulate matter, Sterility. Compliance to the standard was established using batch analysis data and stability data.

Stability and container closure system

Pzolenov (Pantoprazole for Injection 40 mg):

Stability studies were conducted on 3(three) batches of the finished product stored at 30 ± 2°C, RH: 75 ± 5 % for 24 months and 40℃±2℃ /75%±5%RH for 6 months. Based on the stability data presented, the approved shelf-life is 24 months when stored in Amber glass vial USP type III with storage condition 'Do not store above 30°C , Protect from light & Do not freeze'.

Sodium Chloride Injection BP 0.9% w/v:

Stability studies were conducted on 3(three) batches of the finished product stored at 30 ± 2°C, RH: 75 ± 5 % for 24 months and 40℃±2℃ /75%±5%RH for 6 months. Based on the stability data presented, the approved shelf-life is 24 months when stored in LDPE Plastic Ampoule with storage condition 'Do not store above 30°C'.

Safety and efficacy information

PZOLENOV powder for solution for injection is a parenteral formulation and therefore fulfils the exemption mentioned in the part III: guidelines on therapeutic equivalence requirements, which states that a bioequivalence study is not required if the solutions for injection that contain the same active ingredients and excipients in the same concentrations as currently registered products and which are administered by the same route(s). The quantitative composition of PZOLENOV powder for solution for injection is entirely the same as the reference products in the market. Therefore, it may be considered as therapeutic equivalent, with the same efficacy/safety profile as known for the active substance of the reference medicinal product. The current product can be used instead of its reference product
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4. Benefit-Risk Assessment and Conclusion

On basis of the data submitted, the current state of knowledge and compliance to Good Manufacturing Practice, the benefit of the product outweighs the risks associated with its use when used in accordance to the summary of product characteristics. PZOLENOV powder for solution for injection is recommended for registration.

5. Post-approval updates

Variation applications

Reference number	Date submitted	Change requested	Recommendation	Granting date

Feedback from pharmacovigilance, post marketing surveillance and enforcement activities

Type of feedback	Impact	Response

Re-registration applications

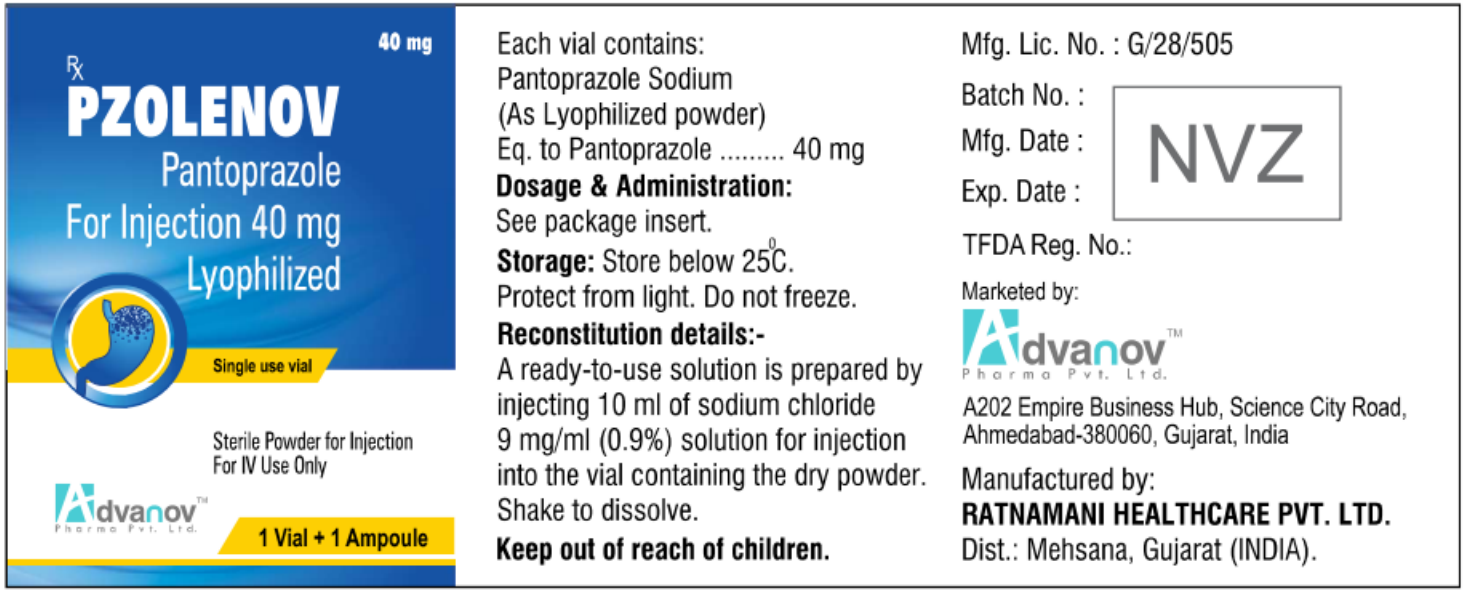
Application for renewal of registration was submitted on <DDMMYYYY>. The application was finalized in <number> rounds of evaluation. The product was confirmed to still be compliant to the standards of quality, safety and efficacy, hence registration was renewed on <DDMMYYYY>.

PART 5: CHANGE HISTORY

Version number	**Date**	**Description of update**	**Section(s) Modified**	**Approval date**

Annex I: Mock up labels;

Primary pack label;



Secondary pack label:

Effective date: 03/10/2022