THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR SITAPRIL 50® (SITAGLIPTIN PHOSPHATE MONOHYDRATE EQUIVALENT TO SITAGLIPTIN 50 MG) FILM COATED TABLETS

Version number 01, 03/01/2023

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1. Introduction

Sitapril 50® is a s a generic medicine of Janumet ® (Sitagliptin Phosphate Monohydrate 50 mg) tablets, Merck Sharp & Dohme (UK) Limited. Sitapril 50® is an Anti-Diabetic medicine belonging to Dipeptidyl peptidase 4 (DPP-4) inhibitors group. Sitapril 50® exerts is activity by increasing the levels of the Incretin hormones Glucagon-like Peptide-1 (GLP- 1) and glucose-dependent insulinotropic polypeptide (GIP). Sitapril 50® is approved in Tanzania for use in adults only.

1.1 Product details

Registration number	TAN 21 HM 0398
Brand name	Sitapril 50®
Generic name, strength and form	Sitagliptin Phosphate Monohydrate 50 mg Film Coated Tablets
ATC classification	ATC Code-A10BH01 Anti-Diabetic, Dipeptidyl peptidase 4 (DPP-4) inhibitors
Distribution category	POM
Country of origin	India
Associated product	Sitapril 25® and Sitapril 100®
Marketing Authorization Holder	Ajanta Pharma Limited Address: Ajanta House, Charkop, Kandivli (W), Mumbai 400067, India
Local Technical Representative	Astra Pharma (T) Limited. Address: Plot no-12, Vingunguti Industrial Area, Nyerere Road, opp: Pepsi tanzania Ltd, Dar -Es- Salaam.

1.2 Assessment procedure

The application for registration of Sitapril 50® was submitted on 29/01/2021. The product underwent full assessment. Assessment was completed in 2(two) rounds of evaluation. Sitapril 50® was registered on 09/10/2021.

1.3 Information for users

Visual description of the finished product	Light beige colored, round, film coated tablets debossed ‘ST2’ on one side and plain on other side
Primary packing material	Alu-Alu blister pack
Secondary packing materials	A printed carton box
Shelf-life and storage condition	24 months, Do not store above 30°C
Route of administration	Oral
Therapeutic indications	Sitagliptin is indicated as an adjunct to diet and

	exercise to improve glycemic control in adults with type 2 diabetes mellitus

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 that is intended for long term use, the package insert contains both full prescribing information as per SmPC and simplified information for patients.

Container labels

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

Brand name: Sitapril 50®

Composition: Sitagliptin Phosphate Monohydrate equivalent to Sitagliptin 50 mg

Pack size: 30 tablets

Manufacturing details: batch number, manufacturing date, expiry date

Storage conditions: Do not store above 30°C

Manufacturer address: Ajanta Pharma Limited, B-4-5-6, MIDC Industrial Area, Paithan, Aurangabad, 431148, Dist: Aurangabad, Maharashtra, India.

Unique identifier: N/A

Special warnings/precautions or instructions for use: Read the patient information Leaflet carefully before use

The details of the primary pack include:

Brand name and strength: Sitapril 50®

Manufacturing details: batch number, manufacturing date, expiry date

Name of manufacturer: Ajanta Pharma Limited

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(s)

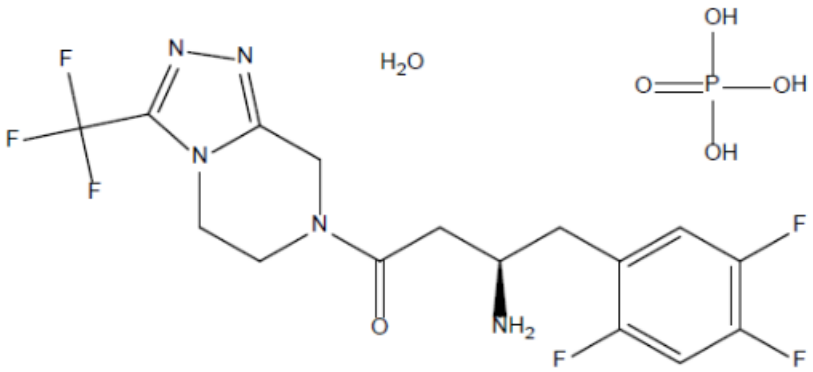
Information on quality of the API was submitted in form of Full details.

General properties
Sitagliptin Phosphate Monohydrate API is compendia in USP/BP.

Molecular formula: $C_{16}H_{15}F_6N_5OH_3PO_4H_2O$

Chemical name: 7-[(3R)-3-Amino-1-oxo-4-(2,4,5-trifluorophenyl) butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-1,2,4-trizolo[4,3-a] pyrazine phosphate monohydrate

Structure:



Critical physico-chemical properties are:

The active substance is White to off-white crystalline powder Soluble in water and N, N-Dimethyl formamide, slightly soluble in methanol and insoluble in2-propanol. It is not known to exhibit polymorphism or to form defined hydrates.

Manufacture
The API manufacturing site, MSN Pharmachem Private Limited, Plot No.: 212 / A,B,C,D, Phase-II, IDA Pashamylaram, Pashamylaram (Village), Patancheru (Mandal), Sangareddy District,Telangana, Pin code: 502 307, India was noted to comply with WHO GMP requirements as evidenced by the GMP certificate issued by Drugs Control Administration of Government of Telangana. Sitagliptin Phosphate Monohydrate 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 USP standards and ICHQ3A. The parameters monitored during quality control are: description (visual), solubility, identification (IR, HPLC, and Phosphates), assay (HPLC), related substances (HPLC), enantiomeric purity (HPLC), residual solvents (GC), water content (KF), solid state (XRPD), particle size distribution (laser diffraction), bulk density, phosphate content. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The shelf-life period of Sitagliptin Phosphate Monohydrate API is 60 months when packed in stored in the original packing material and stored at controlled room temperature between 20°C and 25°C (excursions allowed between 15°C and 30°C).

Quality of the Finished Pharmaceutical Product

Formulation

Sitapril 50® is a light beige colored, round, film coated tablets debossed 'ST2' on one side and plain on other side.

Sitapril 50® contains Sitagliptin Phosphate Monohydrate and other ingredients listed here after: Microcrystalline Cellulose, Anhydrous Dibasic Calcium Phosphate, Croscarmellose Sodium, Magnesium Stearate, Sodium Stearyl Fumarate, Instacoat Aqua II A02G10251 Beige (Polyvinyl Alcohol, Polyethylene Glycol 3350, Talc, Titanium Dioxide, Yellow Iron Oxide and Red Iron Oxide), Purified water. The quantities of all ingredients are confirmed to be in line with the recommendations of Handbook of Pharmaceutical Excipients, Edition 8^{th} in terms of function and quantities.

Manufacture

The finished product was manufactured at Ajanta Pharma Limited, B-4-5-6, MIDC Industrial Area, Paithan, Aurangabad, 431148, Dist: Aurangabad, Maharashtra, India. The compliance of the site to TMDA GMP standards was confirmed through site inspection on DD/MM/YY.

Specifications

The FPP is BP/USP. The manufacturer controls the quality of the finished product as per USP standards and ICH requirements. The parameters monitored during quality control are: description (visual), identity of API (IR and HPLC), assay (HPLC), average weight, uniformity of dosage (weight variation), dissolution (HPLC), water (KF), disintegration, elementary impurities, microbial enumeration tests, and test for specified microorganisms. Compliance to the standard was established using batch analysis data and stability data.

Stability and container closure system

Stability studies were conducted on three (3) batches of the finished product stored at 30^0 ± 2°C & 75% ± 5% RH for 24 months and 40^0 ± 2°C & 75% ± 5% RH for 6 months. Based on the

stability data presented, the approved shelf-life is 24 months when stored in Alu-Alu blister pack at Do not store above 30°C.

Safety and efficacy information

The biowaiver was approved based on additional strength.

Sitapril 50® fulfilled the criteria for waiving an in-vivo bioequivalence study as per relevant TMDA guidance. Dissolution profiles of Sitapril 50® (50 Sitagliptin (as phosphate monohydrate)) tablets was compared to Sitapril 100® (100 Sitagliptin (as phosphate monohydrate)) tablets. At least 85% of the labelled amount of Sitagliptin had dissolved in all three media. Therefore, confirming similarity.

4. Benefit-Risk Assessment and Conclusion

On basis ofthe 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. Sitapril 50® 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 label

Primary label:

Actual Blister Size : 117 x 69 mm

Effective date: 03/10/2022

Secondary label

Actual Size : 124 x 23 x 73 mm