TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR A-GLIP (SITAGLIPTIN PHOSPHATE MONOHYDRATE 50 mg) FILM COATED TABLETS

Version number 1.0
11th April, 2022

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1. Introduction

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

1.1 Product details

Registration number	TAN 22 HM 0144
Brand name	A-GLIP
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	Pakistan
Associated product	
Marketing Authorization Holder	ATCO Laboratories B – 18, S. I. T. E, Karachi, 75700 Pakistan
Local Technical Representative	Samiro Pharmaceuticals Limited, Uhuru Street, Kariakoo, P.O. Box 38062, Dar es Salaam.

1.2 Assessment procedure

The application for registration of GLIP was submitted on 29th June 2018. The product underwent full assessment. Assessment was completed in five rounds of evaluation. GLIP (Sitagliptin Phosphate Monohydrate 50 mg) Tablets was registered on 11th April 2022

1.3 Information for users

Visual description of the finished product	Light orange, round, biconvex, film coated tablet having bisect line on one side and other side plain
Primary packing material	Alu -Alu blister pack, pack of 14's
Secondary packing materials	Printed cardboard box
Shelf-life and storage condition	24 months
Route of administration	Oral
Therapeutic indications	Sitagliptin Phosphate Monohydrate 50mg tablet is indicated for adult patients 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, 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: A-GLIP
Composition: Sitagliptin Phosphate Monohydrate 50 mg, list of excipients: Povidone, Magnesium Stearate, Ferric Oxide Yellow, Microcrystalline Cellulose, Croscarmellose Sodium, Lactose Anhydrous, Opadry Y.1.7000, Ferric Oxide, Purified Water.

Pack size: 1 x 14's tablets

Manufacturing details: batch number, manufacturing date, expiry date

Storage conditions: Do not store above 30°C

Manufacturer address: ATCO Laboratories, B – 18, S. I. T. E, Karachi, 75700 Pakistan

Unique identifier: Not applicable

Special warnings/precautions or instructions for use: Refer the leaflet

The details of the primary pack include:

Brand name and strength: A-GLIP

Manufacturing details: <batch number, manufacturing date, expiry date>

Name of manufacturer: ATCO Laboratories, B – 18, S. I. T. E, Karachi, 75700 Pakistan

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.

Describe any approved deviation to the requirements and the justification for the deviation.

Mock labels are appended as annex I.

3. Scientific discussion

Quality of Active Pharmaceutical Ingredient(s)

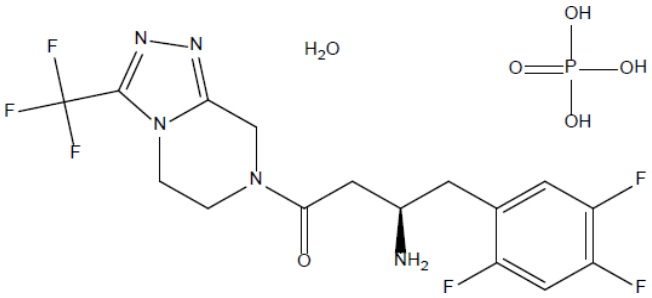
Information on quality of the API was submitted in form of DMFs

General Information
Sitagliptin Phosphate Monohydrate

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:



physico-chemical properties of the Active Substance

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 is Beijing Huikang Boyuan Chemica, Tech Co., LTD., Fluoride Industrial Park, Fuxin City, Liaoning Province-123000, China. The manufacturing site was complying with GMP requirements as evidenced by the GMP certificate issued by Drug Control Administration People's Republic of China. 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, identification by (IR and HPLC), water content (USP), sulfate (USP), chloride (USP), heavy metals (USP), residual solvents by (GC), related substances (USP) and assay (USP). Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system
The re-test period of Sitagliptin Phosphate Monohydrate API is 24 months when packed in double polyethylene bags in HDPE container and stored below 25°C

Quality of the Finished Pharmaceutical Product

Formulation
A-GLIP (Sitagliptin Phosphate Monohydrate 50 mg) is a Light orange, round, biconvex, film coated tablet having bisect line on one side and other side plain

A-GLIP contains Sitagliptin Phosphate Monohydrate and other ingredients listed here after: Povidone, Magnesium Stearate, Ferric Oxide yellow, Microcrystalline Cellulose, Croscarmellose Sodium, Lactose Anhydrous, Opadry Y.1.7000, Ferric Oxide, Purified Water. The quantities of all ingredients are confirmed to be in line with the recommendations of Handbook of Pharmaceutical Excipients 8th Edition in terms of function and quantities.

Manufacture
The finished product was manufactured at ATCO Laboratories, B – 18, S. I. T. E, Karachi, 75700 Pakistan. The compliance of the site to TMDA GMP standards was confirmed through site inspection on 1st and 2nd November, 2017.

Specifications
The FPP is compendia in BP/USP. The manufacturer controls the quality of the finished product as per in-house and ICHQ3B requirements. The parameters monitored during quality control are: Description, identification, uniformity of weight, dissolution, related substances and assay. Compliance to the standard was established using batch analysis data and stability data.

Stability and container closure system
Stability studies were conducted on three batches of the finished product stored at 30 ± 2°C, 75 ± 5% RH for 24 months and 40 ± 2ºC, 75 ± 5% RH for 6 months. Based on the stability data presented, the approved shelf-life is 24 months when stored in Alu- Alu blisters, packed in a printed carton with a storage condition “Do not store above 30^0C”

Safety and efficacy information

Safety and efficacy of A-GLIP was established through biowaiver application.

The biowaiver was approved based on BCS classification.

A-GLIP fulfilled the criteria for waiving an in-vivo bioequivalence study as per relevant TMDA guidance. Dissolution profiles of A-GLIP (Sitagliptin Phosphate Monohydrate 50 mg) was compared to Januvia 50 (Sitagliptin phosphate Tablets 50mg) marketed by Merk Sharp & Dohme (UK) Limited. At least 85% of the labelled amount of Sitagliptin Phosphate Monohydrate had dissolved in all three media. Therefore, confirming similarity

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. A-GLIP 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