TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR NEOGLIP (SITAGLIPTIN + METFORMIN 50/1000 MG) TABLETS

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1. Introduction

Neoglip is a generic medicine of Sitagliptin Phosphate and Metformin Hydrochloride. Neoglip is a antidiabetic medicine belonging to the combinations of oral blood glucose lowering drugs group. Neoglip exerts is activity by reducing blood glucose levels. Sitagliptin works by inhibition of dipeptidyl-peptidase-4 thus reducing the activation of incretin hormones. Metformin improves glucose tolerance and reduces plasma glucose levels. Neoglip is approved in Tanzania for use in adults.

1.1 Product details

Registration number	TAN 21 HM 0054
Brand name	Neoglip
Generic name, strength and form	Sitagliptin phosphate 50 mg/Metformin hydrochloride 1000 mg
ATC classification	A10BD07
Distribution category	Prescription Only Medicine
Country of origin	Pakistan
Associated product	Neoglip 50/500 mg
Marketing Authorization Holder	Atco Laboratories
Local Technical Representative	Samiro Pharmaceuticals Limited

1.2 Assessment procedure

The application for registration of Neoglip was submitted on 20/06/2017. The product underwent full assessment. Assessment was completed in three (3) rounds of evaluation. Neoglip was registered on 24/12/2020.

1.3 Information for users

Visual description of the finished product	Off-white, oblong, biconvex film coated tablets having ATCO engraved on one side and other side plain
Primary packing material	Aluminium blisters of 7's
Secondary packing materials	Blisters in a carton box
Shelf-life and storage condition	Do not store above 30oC. Protect from light, heat & moisture
Route of administration	Per oral
Therapeutic indications	Management of type 2 diabetis

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 prescription only medicine 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: Neoglip

Composition: Sitagliptin 50 mg + Metformin HCl 1000 mg tablets)

Pack size: 14 tablets

Manufacturing details: batch number, manufacturing date, expiry date

Storage conditions: Do not store above 30oC. Protect from light, heat & moisture

Manufacturer address: ATCO Laboratories Limited, B-18, S.I.T.E, Karachi-Pakistan

Unique identifier: Not included. Notification to be sent to applicant

Special warnings/precautions or instructions for use: <Not applicable>

The details of the primary pack include:
Brand name and strength:

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

Name of manufacturer: <name only>

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/currently not available>.

3. Scientific discussion

Quality of Active Pharmaceutical Ingredient(s)

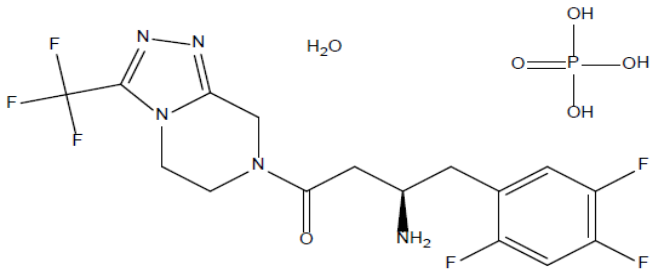
Sitagliptin API
Information on quality of the API was submitted in form of full details as per compendia requirements.

General properties
Molecule API is compendia in USP.

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:



Manufacture

The API manufacturing site, Beijing Huikang Boyuan Chemica Tech. Co. Limited, 7 Haiying Road, Science City, Fengtai District, Beijing -100070, China was noted to comply with WHO GMP requirements as evidenced by the GMP certificate issued by the Lioning Province. Sitagliptin 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: Appearance, Solubility, Identification, Water content, Sulphated ash, Heavy metals, Phosphoric acid content, Assay and Related impurities (single impurity and total impurity). Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The shelf-life period of Sitagliptin API is 24 months when packed in polyethylene bags and stored at 25°C.

Metformin Hydrochloride

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

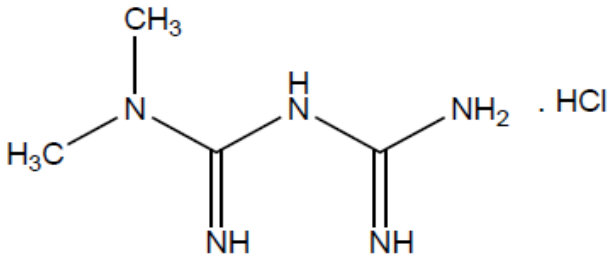
General properties

Metformin Hydrochloride API is compendia in European Pharmacopeia and USP.

Molecular formula: $C_4H_{11}N_5.HCl$

Chemical name: 1,1-dimethylbiguanide hydrochloride
N,N-dimethylimidodicarbonimidic.
N,N-dimethyldiguanide hydrochloride
N-dimethylguanylguanidine hydrochloride

Structure:



Critical physico-chemical properties of the API were polymorphism. Confirmation that the API produced is of Amorphous form was confirmed by X-ray powder diffraction.

Manufacture

The API manufacturing site, Abhilash Chemicals and Pharmaceuticals Pvt. Ltd. 34/6A, Nayakkanpatti village, Madurai North Taluk, Madurai, India was noted to comply with WHO GMP requirements as evidenced by the GMP certificate issued by the office of the Director of Drugs Control, Tamil nadu. Metformin HCl 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 European Pharmacopeia standards and ICHQ3A. The parameters monitored during quality control are: identification, appearance of solution, impurity F, impurity A, any other impurity and total impurities. Other parameters were heavy metals, sulphated ash, assay, residual solvents and loss on drying. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The shelf-life period of Metformin API is 24 months when packed in low density polyethylene bags and stored at 25°C .

Quality of the Finished Pharmaceutical Product

Formulation

Neoglip is an off-white, oblong, biconvex film coated tablet having ATCO engraved on one side and other side plain. 14 tablets are packed in Alu/Alu blisters. Neoglip contains Sitagliptin Phosphate and Metformin Hydrochloride and other ingredients listed here after: microcrystalline cellulose, povidone, croscarmellose sodium, sodium lauryl sulphate, magnesium stearate, purified water and Opadry white. The quantities of all ingredients are confirmed to be in line with the recommendations of Handbook of Pharmaceutical Excipients, Edition 7 in terms of function and quantities.

Manufacture

The finished product was manufactured at ATCO Laboratories Limited, Plot No. B-18, S.I.T.E., Karachi-75700, Pakistan. The compliance of the site to TMDA GMP standards was confirmed through site inspection.

Specifications

The FPP as a fixed dose combination medicine is non-compendia. The manufacturer controls the quality of the finished product as per in-house standards, general chapters of British Pharmacopeia and USP as well as ICHQ3B requirements. The parameters monitored during

quality control are: description, uniformity of weight, disintegration time, identification, assay, dissolution and uniformity of dosage units. 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°C ± 2°C, relative humidity 65 % ± 5 % for 24 months and 40°C ± 2°C, relative humidity 75 % ± 5 % for 6 months. Based on the stability data presented, the approved shelf-life is <24> months when stored in aluminium blisters at 30°C.

Safety and efficacy information

Safety and efficacy of Neoglip was established through biowaiver application.

In case of biowaiver

The biowaiver was approved based on BCS classification.

Neoglip fulfilled the criteria for waiving an in-vivo bioequivalence study as per relevant TMDA guidance. Dissolution profiles of Neoglip 50/1000 mg film coated tablets was compared to Janumet 50/1000 mg tablets marketed by Merkc, Sharpe & Dohme Limited. At least 85% of the labelled amount of Sitagliptin had dissolved in 15 minutes for all three media. Similarly, at least 85% of the labelled amount of Metformin had dissolved in 15 minutes for all three media.

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. Neoglip is recommended for registration.

5. Post-approval updates

Variation applications

Reference number	Date submitted	Change requested	Recommendation	Granting date
Nil	Nil	Nil	Nil	Nil

Feedback from pharmacovigilance, post marketing surveillance and enforcement activities

Type of feedback	Impact	Response
Nil	Nil	Nil

Re-registration applications

NA

PART 5: CHANGE HISTORY

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

Annex I: Mock up label