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MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR PHYLLINE (AMINOPHYLLINE 250 MG/10 ML) SOLUTION FOR INJECTION

Version number 1.0
21 October 2023

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1. Introduction

Phylline is a generic medicine of Aminophylline solution for injection. Phylline is a bronchodilator medicine belonging to R03DA05- Xanthines group. Phylline exerts is activity by relaxing smooth muscle and relieving bronchial spasm, stimulating the myocardium and reducing venous pressure in congestive heart failure, leading to a marked increase in cardiac output.It has stimulant effect on respiration, and also a diuretic action of short duration. Phylline is approved in Tanzania for use in adults and children.

1.1 Product details

Registration number	TAN 20 HM 0415
Brand name	Phylline
Generic name, strength and form	Aminophylline 250mg/10ml solution for injection
ATC classification	R03DA05- Xanthines
Distribution category	POM
Country of origin	India
Associated product	State any other product of formulation, strength or site that is linked or associated with the product if applicable
Marketing Authorization Holder	Swiss Parenterals Limited. Regi. Office 304,Samaan II, Opp. Shell petrol pump, Nr. Prahaladnagar, Garden, Anandnagar Road , Ahmedabad-380 015, Gujarat - INDIA
Local Technical Representative	Planet Pharmaceutical Limited, P. O. Box 38328,Vingunguti, Dar es Salaam, Tanzania.

1.2 Assessment procedure

The application for registration of Phylline was submitted on 18/11/2019. The product underwent full assessment. Assessment was completed in 2 rounds of evaluation. Phylline was registered on 25/09/2020.

1.3 Information for users

Visual description of the finished product	A clear colourless solution, free from visible particles and fibers
Primary packing material	Glass ampoule of 1 x 10 ml
Secondary packing materials	
Shelf-life and storage condition	24 Months Store below 30^0C**,** Protect from light
Route of administration	Intravenous
Therapeutic indications	Disease of the cardiovascular system (e.g. an

	adjunct in the treatment of pulmonary oedema or paroxysmal nocturnal dyspnoea caused by left ventricular heart failure), reversible airways obstruction including status asthmaticus and acute bronchospasm

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 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: Phylline
Composition: Aminophylline injection 250 mg/10 ml, excipients - ethylene glycol
Pack size: 10 ml
Manufacturing details: batch number, manufacturing date, expiry date
Storage conditions: Store below 30^0C, in a dry place, protect from light
Manufacturer address: Swiss Parenterals Limited. 808,809 & 810 Kerala Industrial Estate, G.I.D.C., Nr. Bavla, Dist. Ahmedabad-382 220, Gujarat - INDIA.
Unique identifier: <state the unique identification used>
Special warnings/precautions or instructions for use: <include warnings or IFU if applicable>

The details of the primary pack include:
Brand name and strength: Phylline(Aminophylline injection 250 mg/10 ml)
Manufacturing details: batch number, manufacturing date, expiry date
Name of manufacturer: Swiss Parenterals Limited

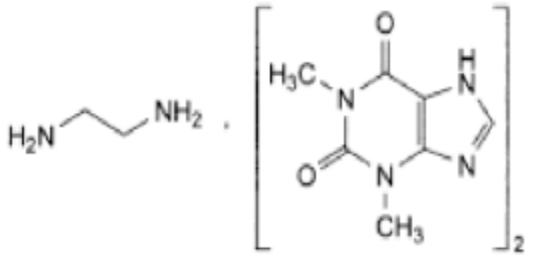
The content of the primary and secondary labels was aligned to the requirements of the Part V of the Compendium: Guidelines on Format and Content of Product Labels for Medicinal products. The label contains sufficient information for proper identification of the medicine and post marketing follow up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

3. Scientific discussion

Quality of Active Pharmaceutical Ingredient(s)

Information on quality of the API was submitted in form of APIMF.

General properties
Aminophylline API is compendia in USP/BP.
Molecular formula: $C_{16}H_{24}N_{10}O_4$
Chemical name: 1, 3-Dimethyl-7H-purine-2,6-dione; ethane-1,2-diamine
Structure:



Critical physico-chemical properties of the API were freely soluble in water, practically insoluble in anhydrous ethanol.

Manufacture
The API manufacturing site, Aarti Industries Limited, Unit – III Plot no. K – 17/18/19, MIDC, Tarapur, Tal.& Dist: Palghar Pin – 401 506, Maharashtra, India was noted to comply with WHO GMP requirements as evidenced by the GMP certificate issued by Food & Drugs Administration (Maharashtra State), India. Aminophylline 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 BP standards and ICHQ3A. The parameters monitored during quality control are: description, solubility, identification, appearance of solution, related substances,water ,sulphated ash, assay. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system
The re-test period of Aminophylline API is 36 months when packed in polyethylene bags and stored at below 30^0C.

Quality of the Finished Pharmaceutical Product

Formulation

Phylline is a a clear colourless solution, free from visible particles and fibers. Phylline contains Aminophylline and other ingredients listed hereafter ethylene diamine,water for injections. The quantities of all ingredients are confirmed to be in line with the recommendations of Handbook of Pharmaceutical Excipients, Edition <number> in terms of function and quantities. Ingredient, <excipient> is of safety concern therefore appropriate warnings were included in the product label.

Manufacture

The finished product was manufactured at Swiss Parenterals Ltd, 808,809 & 810 Kerala Industrial Estate, Nr. Bavla, Dist. Ahmedabad - 382 220, Gujarat, INDIA. The compliance of the site to TMDA GMP standards was confirmed through site inspection on <date of GMP compliance>.

Specifications

The FPP is compendia in BP. The manufacturer controls the quality of the finished product as per BP and ICHQ3B requirements. The parameters monitored during quality control are: description, identification, extractable volume, pH sterility, bacterial endotoxins, particulate matter, 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 3 batches of the finished product stored at 30ºC±2ºC, 75% RH±5% for 24 months and 40°C ± 2°C, 75% RH ±5% for 6 months. Based on the stability data presented, the approved shelf-life is 24 months when stored in 10 ml plain glass ampoule at below 30^0C.

Safety and efficacy information

Studies were not submitted as Phylline is a solution for injection with the same composition as the reference product.

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. Phylline 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

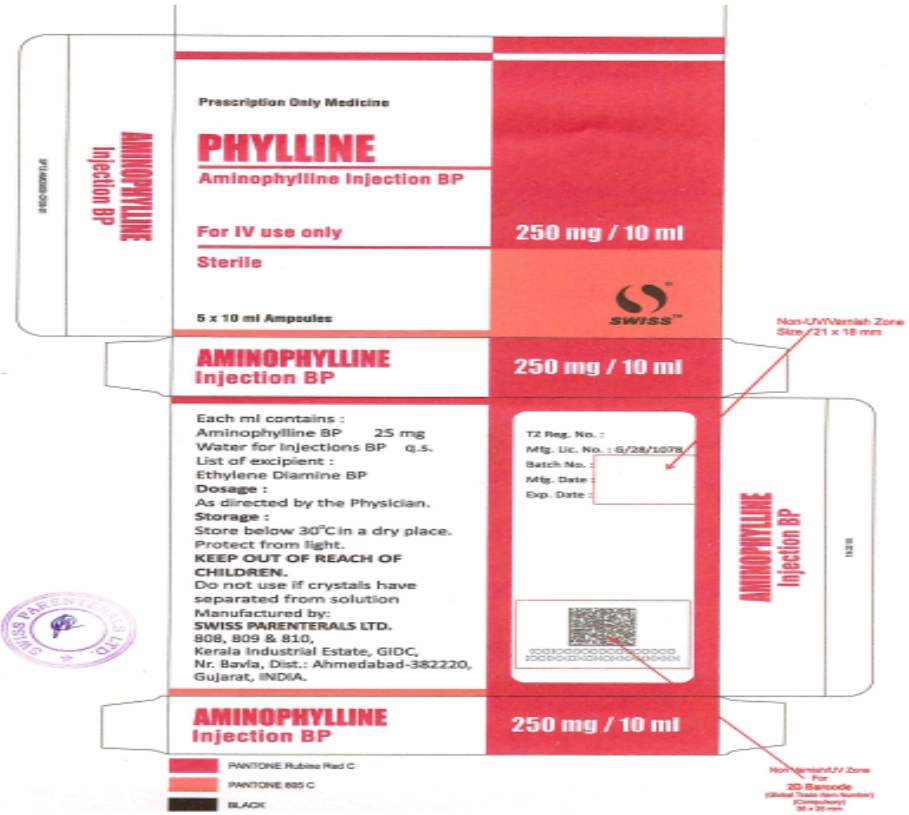
Re-registration applications

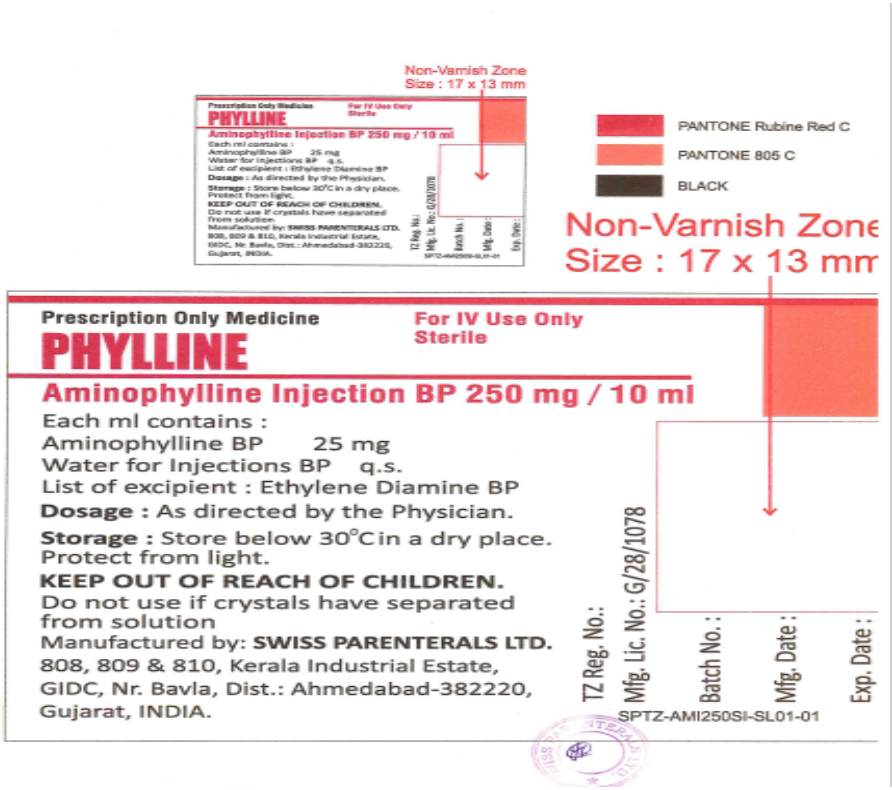
Application for renewal of registration was submitted on <DDMMYYYY>. The application was finalized in <number> rounds of evaluation. The product was confirmed to still be compliant to the standards of quality, safety and efficacy, hence registration was renewed on <DDMMYYYY>.

PART 5: CHANGE HISTORY

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

Annex I: Mock up label




Non-Varnish Zone
Size : 17 x 13 mm
PANTONE Rubine Red C
PANTONE 805 C
BLACK
Non-Varnish Zone
Size : 17 x 13 mm
Prescription Only Medicine
For IV Use Only
Sterile
PHYLLINE
Aminophylline Injection BP 250 mg / 10 ml
Each ml contains :
Aminophylline BP 25 mg
Water for Injections BP q.s.
List of excipient : Ethylene Diamine BP
Dosage : As directed by the Physician.
Storage : Store below 30°C in a dry place.
Protect from light.
KEEP OUT OF REACH OF CHILDREN.
Do not use if crystals have separated
from solution
Manufactured by: SWISS PARENTERALS LTD.
808, 809 & 810, Kerala Industrial Estate,
GIDC, Nr. Bavla, Dist.: Ahmedabad-382220,
Gujarat, INDIA.
TZ Reg. No.:
Mfg. Lic. No.: G/28/1078
Batch No. :
Mfg. Date :
Exp. Date :
SPTZ-AMI250SI-SL01-01