THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR ARTISURGE 60 (ARTESUNATE 60 MG) POWDER FOR INJECTION AND DILUENTS (STERILE SODIUM BICARBONATE 2ML & 0.9% CELINE FOR INJECTION, 10ML)

Version number 1.0
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1. Introduction

ARTISURGE 60 is an artemsinin derivative medicine belonging to P01BE03 - Artemisinin and derivatives, plain group. ARTISURGE 60 exerts is activity by causing cleavage of endoperoxide bridge in the pharmacophore of DHA and therefore generates reactive oxygen species (ROS), which increases oxidative stress and causes malarial protein damage via alkylation. In addition, Artesunate potently inhibits the essential Plasmodium falciparum exported protein 1 (EXP1), a membrane glutathione S-transferase. As a result, the amount of glutathione in the parasite is reduced. ARTISURGE 60 is approved in Tanzania for use in adults and children.

1.1 Product details

Registration number	TAN 23 HM 0291
Brand name	ARTISURGE 60
Generic name, strength and form	Each vial contains Artesunate 60mg, powder for injection
ATC classification	Antithrombotic agent, heparin group, ATC code: B01A B05
Distribution category	POM
Country of origin	Pakistan
Associated product	ARTISURGE 120
Marketing Authorization Holder	Surge Laboratories (Pvt). Ltd., 10th Km, Faisalabad Road, Bikhi
Local Technical Representative	Core Pharma P.O. Box 21412, Dar Es Salaam

1.2 Assessment procedure

The application for registration of ARTISURGE 60 was submitted on 06/11/2021. The product underwent full assessment. Assessment was completed in 3 (three) rounds of evaluation and the product was registered on 01/06/2023.

1.3 Information for users

Visual description of the finished product	A fine, White crystalline powder filled in vial
Primary packing material	7 ml Clear Tubular Glass Vials (USP Type-I) with 20mm Bromobutyl Rubber Stoppers
Secondary packing materials	A printed carton box
Shelf-life and storage condition	24 months with storage conditions ‘Do not store above 30℃. Protect from heat, light and moisture’
Route of administration	Intravenous and Intramuscular Injection
Therapeutic indications	Artisurge Injection is indicated for the initial treatment of severe malaria in adult and pediatric patients. Treatment of severe malaria with Artisurge Injection should always be followed by a complete treatment course of an appropriate oral antimalarial regimen.

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: ARTISURGE 60

Composition: Each vial contains Artesunate 60mg

Pack size: 1vial

Manufacturing details: batch number, manufacturing date and expiry date

Storage conditions: Do not store above 30℃. Protect from heat, light and moisture

Manufacturer address: physical address of release site

Unique identifier: Not applicable

Special warnings/precautions or instructions for use: As directed by the doctor, For details| please see enclosed leaflet

The details of the primary pack include:

Brand name and strength: ARTISURGE 60

Manufacturing details: batch number, manufacturing date and expiry date

Name of manufacturer: Surge Laboratories (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 Substance

Information on quality of the active substance was submitted in form of DMF.

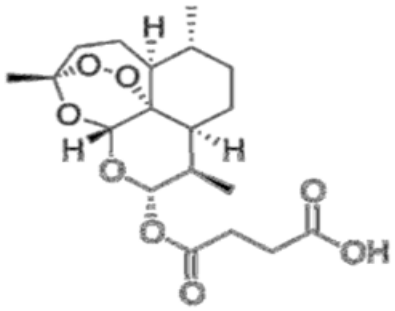
General Information

Artesunate drug substance I is Ph.Int.

Molecular formula: $C_{19}H_{28}O$

Chemical name:
(3R,5aS,6R,8aS,9R,10S,12R,12aR)-3,6,9-trimethyldecahydro-3,12-epoxy-12H-pyrano[4,3-J] 1,2-benzodioxepin-10-yl hydrogen butanedioate

Structure:



General properties

Artesunate is slightly soluble in water, very soluble in dichloromethane, freely soluble in ethanol (~750g/l) & acetone. Artesunate API was considered as a highly soluble API as it has Dose/solubility volume of less than 250 ml. The drug product will be administered in solution form and hence physical properties like polymorphism and PSD are not critical

Manufacture

Artesunate active substance manufacturer is MICRO ORGO-CHEM, C-1/B-57, LIC Sector, GIDC, Vapi-396 195, Gujarat, India. The manufacturing complies with GMP requirements as evidenced by the GMP certificates issued by Gujarat Food and Drug Control Administration. Artesunate active substance 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 International Pharmacopoeia and ICH guidelines. The parameters monitored during quality control are: description, solubility, identification by HPLC and IR, specific optical rotation, bacterial endotoxins, pH, water, heavy metals, sulphated ash, assay, sterility, and residual solvents. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The retest period of Artesunate active substance is 60 months respectively when packed in virgin, food grade, nontoxic, double low density polyethylene bag (LDPE bag) at the intended storage condition of 25 °C.

Quality of the Drug Product

Formulation

ARTISURGE 60 is a fine, White crystalline powder filled in vial.

ARTISURGE 60 contains the API Artesunate. Diluents: 2 mL Sterile Sodium Bicarbonate + 10 mL ampoule of sterile Saline 0.9%.

Manufacture

The finished product manufacturer is Surge Laboratories (PVT) LTD.,10th Km, Faisalabad Road, Bikhi, District Sheikhupura-Pakistan. The compliance of the site to TMDA GMP standards was confirmed through site inspection on DD/MM/YYYY.

Specifications

The finished product is compendia. The manufacturer controls the quality of the finished product as per International Pharmacopoeia standards and ICH requirements. The parameters monitored during quality control are: description, identification by IR and HPLC, pH, bacterial endotoxins, particulate matter, sterility, assay, constituted solution, crystallinity, uniformity of dosage units, and sterility. Compliance to the standard was established using batch analysis data and stability data.

Stability and container closure system

Stability studies were conducted on 3 (three) batches of the finished product stored at 30°C ± 2°C, 75 % ± 5% RH for 36 months and 40°C ± 2°C, 75 % ± 5% RH for 6 months. Based on the stability data presented, the approved shelf-life is 24 months when stored in 15ml Clear Tubular Glass Vials (USP Type-I) with 20mm Bromobutyl Rubber Stoppers with storage conditions ‘Do not store above 30℃. Protect from heat, light and moisture’.

Safety and efficacy information

ARTISURGE 60 Powder for injection is a parental formulation and therefore fulfils the exemption for demonstrating therapeutic. The composition of ARTISURGE 60 powder for injection manufactured by Surge Laboratories (Pvt) Ltd is the same as the originator product, Artesunate Powder for injection manufactured by Guilin Pharmaceuticals Limited. Therefore, it was considered as therapeutic equivalent, with the same efficacy/safety profile as known for the active substance of the reference medicinal product

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. ARTISURGE 60 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

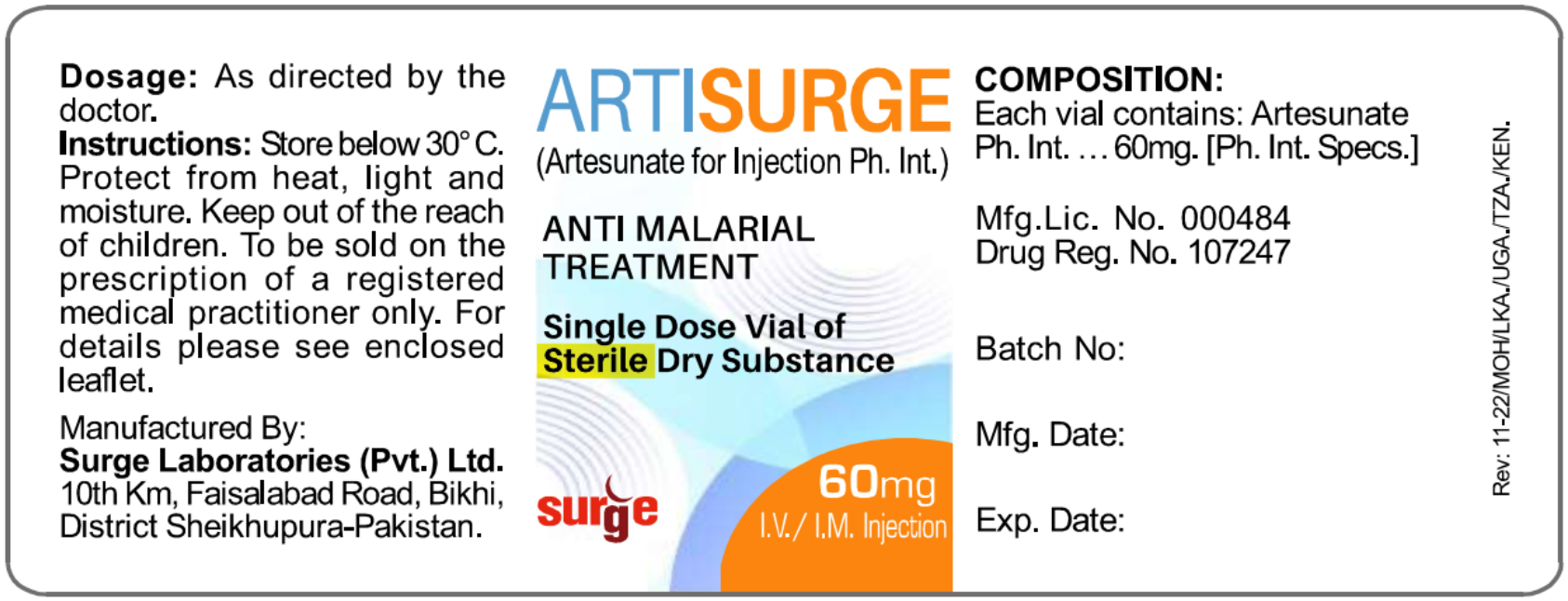
Application for renewal of registration was submitted on <DDMMYYYY>. The application was finalized in <number> rounds of evaluation. The product was confirmed to still be compliant to the standards of quality, safety and efficacy, hence registration was renewed on <DDMMYYYY>.

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: