THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR GLUMAC (ARTEMETHER 80 MG AND LUMEFANTRINE 480 MG) TABLETS

Version number 01

3rd January, 2023

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1. Introduction

Glumac is a generic medicine of Coartem. Glumac is an antimalarial medicine belonging to **P01BF01** antiparasitic products, insecticides and repellents, Antiprotozoal, Antimalarials Artemisinin and derivatives, combinations group. Glumac contains a fixed combination of 2 antimalarial active ingredients, artemether, an artemisinin derivative, and lumefantrine. Both components are blood schizontocides. Glumac is approved in Tanzania for use in adults, children and elderly.

1.1 Product details

Registration number	*TAN 21 HM 0167*
Brand name	*Glumac*
Generic name, strength and form	*Artemether 80 mg and Lumefantrine 1480 mg*
ATC classification	***P01BF01 -** antiparasitic products, insecticides and repellents, Antiprotozoal, Antimalarials Artemisinin and derivatives, combinations*
Distribution category	*POM*
Country of origin	*China*
Associated product	*Not Applicable*
Marketing Authorization Holder	*Shanghai Fosun Pharmaceutical Development Co., Ltd.* *Room 350, No. 25 Kangshi road, Kangqiao town, Pudong New District (Kangqiao), Shanghai* *China.*
Local Technical Representative	*Tridem Pharma Tanzania Limited*

1.2 Assessment procedure

The application for registration of *Glumac* was submitted on *26/07/2020*. The product underwent *abridged assessment*. Assessment was completed in *four* rounds of evaluation. *Glumac* was registered on *29th March, 2021*.

1.3 Information for users

Visual description of the finished product	*Yellow capsule-shaped tablet, debossed with a score line on one side*
Primary packaging material	*Polyvinyl Chloride (PVC)/ Polyvinyl Dichloride (PVDC) and Aluminum foil, heat-sealed*
Secondary packaging materials	*Carton box alongside with a package insert* *640boxes/carton*

	20 blisters/box, 70boxes/carton
Shelf-life and storage condition	*24 months* *Do not store above 30℃, store in the original package in order to protect from moisture*
Route of administration	*Oral*
Therapeutic indications	*Used for the treatment of acute uncomplicated malaria infections caused by a parasite called "Plasmodium falciparum". This parasite is a tiny organism made-up of one cell that is found inside red blood cells.*

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,* 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: *Glumac*
Composition: *Artemether 80 mg and Lumefantrine 480 mg* and the following excipients:

1. *Microcrystalline Cellulose PH102 (USP)*
2. *Polysorbate 80 (USP)*
3. *Hypromellose E6 (USP)*
4. *Croscarmellose sodium (USP)*
5. *Colloidal Silicon Dioxide (USP)*
6. *Talc (USP)*
7. *Magnesium Stearate (USP)*
8. *Purified water (removable) (Ph. Int. & Ch. P & USP & In-house)*

Pack size: *1 x 6 tablets/blister and 2 x 6 tablets/blister*

Manufacturing details:

Storage conditions: *Do not store above 30℃, store in the original package in order to protect from moisture*

Manufacturer address: *Guilin Pharmaceutical Co., Ltd, No. 43 Qilidian Road, China*

Unique identifier: *TMDA registration number*
Special warnings/precautions or instructions for use: *Not Applicable*

The details of the primary pack include:
Brand name and strength: *Glumac 80 mg/480 mg*
Name of manufacturer: *Guilin Pharmaceutical Co., 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

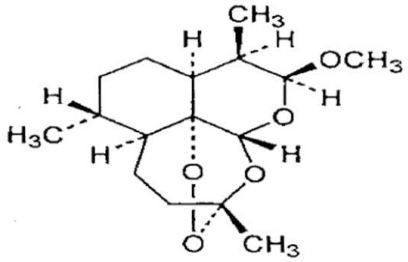
3. Scientific discussion

Quality of Active Pharmaceutical Ingredient(s)

1. Artemether

Information on quality of the API was submitted in form of *proof of WHO prequalification and corresponding requirements as per Compendia.*

General properties
Artemether API is compendia in *International Pharmacopeia*
Molecular formula: $C_{16}H_{26}O_5$
Chemical name: *(3R,5aS,6R,8aS,9R,10S,12R,12aR)-Decahydro-10-methoxy-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin*
Structure:



Critical physico-chemical properties of the API:
Artemether manufactured by Mangalam drugs and organics limited shows two crystal form A and B of which polymorph form was confirmed by manufacturer.

The API is practically insoluble in water thus, particle size is of critical concern, FPP manufacturer included test and limit for control of particles size has been included in the API specification

Manufacture

The API manufacturing site, *Mangalam Drugs and Organics Ltd (Site 1: Unit-1, Plot No.187, 2nd Phase, G.I.D.C., Vapi Gujarat, 396195 and Site 2: Plant 2A, 2B and 2C, Unit 2 Plot No.: 1203, 3rd Phase, G.I.D.C, Gujarat 396195, India* was noted to comply with WHO GMP requirements as evidenced by the GMP certificate issued by *Drugs Control Administration (DCA), Gujarat. Artemether* 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 *International Pharmacopeia standards, ICHQ3C and ICHQ3A*. The parameters monitored during quality control are: *description, melting point, specific rotation, identification, and sulphated ash, loss on drying, related substances, particle size distribution, residual solvents, assay and microbial limit*. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The *re-test* period of *Artemether* API is *24* months when packed in *colorless, virgin food grade, transparent LDPE bags, tied with plastic strip and second packing black LDPE bag in HDPE container* and stored at *or below 25℃ in well closed, light resistance containers.*

2. Lumefantrine

Information on quality of the API was submitted in form of *proof of WHO prequalification and corresponding requirements as per Compendia.*

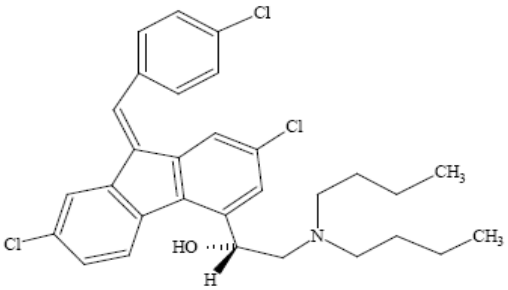
General properties

Artemether API is compendia in *International Pharmacopeia*

Molecular formula: $C_{30}H_{32}Cl_3NO$

Chemical name: *(1RS)-2-(dibutylamino)-1-{(9Z)-2,7-dichloro-9-[(4-chlorophenyl)methylidene]-9H-fluoren-4-yl}ethanol (Racemate)*

Structure:



Critical physico-chemical properties of the API:

Artemether manufactured by Mangalam drugs and organics limited shows a single crystal form-I of which polymorph which was confirmed by manufacturer using pXRD studies.

Lumefantrine occurs as a yellow crystalline powder with a good solubility in chloroform, toluene, methylene dichloride, ethyl acetate and acetone. Lumefantrine is insoluble in water. The solubility profile of the API in various physiological pH was provided. The API is insoluble in water thus, particle size was of critical concern, FPP manufacturer included test and limit for control of particles size in the API specification.

Manufacture

The API manufacturing site, *Mangalam Drugs and Organics Ltd (Site 1: Unit-1, Plot No.187, 2nd Phase, G.I.D.C., Vapi Gujarat, 396195 and Site 2: Plant 2A, 2B and 2C, Unit 2 Plot No.: 1203, 3rd Phase, G.I.D.C, Gujarat 396195, India* was noted to comply with WHO GMP requirements as evidenced by the GMP certificate issued by *Drugs Control Administration (DCA), Gujarat*.

Lumefantrine 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 *International Pharmacopeia standards, ICHQ3C and ICHQ3A*. The parameters monitored during quality control are: *description, melting point, specific rotation, identification, and sulphated ash, loss on drying, related substances, particle size distribution, residual solvents, assay and microbial limit*. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The *shelf life* period of *Lumefantrine* API is *60* months when packed in *two LDPE bags; Primary is white& secondary is black, followed by HDPE drum* and *stored at or below 30℃ in well closed, light resistance containers.*

Quality of the Finished Pharmaceutical Product

Formulation

Glumac is *yellow capsule-shaped tablet, debossed with a score line on one side packed in Polyvinyl Chloride (PVC)/ Polyvinyl Dichloride (PVDC) and Aluminum foil, heat-sealed. Glumac* contains *Artemether/Lumefantrine 80mg/480mg* and other ingredients listed here after:

1. *Microcrystalline Cellulose PH102 (USP)*
2. *Polysorbate 80 (USP)*
3. *Hypromellose E6 (USP)*
4. *Croscarmellose sodium (USP)*
5. *Colloidal Silicon Dioxide (USP)*
6. *Talc (USP)*

7. *Magnesium Stearate (USP)*
8. *Purified water (removable) (Ph. Int. & Ch. P & USP & In-house)*

The quantities of all ingredients are confirmed to be in line with the recommendations of Handbook of Pharmaceutical Excipients, Edition 9 in terms of function and quantities.

Manufacture

The finished product was manufactured at *Guilin Pharmaceutical Co., Ltd of No. 43 Qilidian Road, Guilin Pharmaceutical, Co., Ltd, China.* The compliance of the site to TMDA GMP standards was confirmed through site inspection on *04/06/2020*.

Specifications

The FPP is *International Pharmacopeia*. The manufacturer controls the quality of the finished product as per *International Ph/in-house and ICHQ6A requirements*. The parameters monitored during quality control are: *description, identification, and average tablet weight, friability, content uniformity, and dissolution, loss on drying, related substances, microbial limit 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 6 months* and *40±2°C/75±5% RH for 24 months*. Based on the stability data presented, the approved shelf-life is *24* months when stored in *PVC-PVDC- AL blister as the primary package and paper box as the secondary package* not store above *30℃, store in the original package in order to protect from moisture.*

Safety and efficacy information

The application underwent an abridged review therefore the data under this section were not assessed.

4. Benefit-Risk Assessment and Conclusion

On basis of the data submitted, the current state of knowledge and compliance to Good Manufacturing Practices, the benefit of the product outweighs the risks associated with its use when used in accordance to the summary of product characteristics. *Glumac* was recommended for registration.

5. Post-approval updates

Variation applications

NA

Feedback from pharmacovigilance, post marketing surveillance and enforcement activities

NA

Re-registration applications

NA

PART 5: CHANGE HISTORY

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

Annex I: Mock up label

Glumac® *Tablets* *Comprimés*

Artemether 80mg / Lumefantrine 480mg
Artéméther 80mg / Luméfantrine 480mg

80 mg / 480 mg

Storage: Keep out of the reach and sight of children.
Do not store above 30℃, store in the original package in order to protect from moisture.
Conservation: Tenir hors de la portée et de la vue des enfants.
Ne pas stocker au-dessus de 30℃, conserver dans l'emballage d'origine afin de protéger de l'humidité.

Batch / Lot:

Mfg. / Fab.:

Exp:

Reg. No.:

Marketing Authorisation Holder /
Titulaire de l'Autorisation de Mise sur le Marché :
Shanghai Fosun Pharmaceutical Development Co., Ltd.
Room 350, No.5 Kangshi Road, Kangqiao Town,
Pudong New District (Kangqiao), Shanghai, China.
Bureau 350, N°5 Rue Kangshi, Kangqiao Ville,
Nouveau District de Pudong (Kangqiao),Shanghai, Chine.

6 tablets / blister ×
6 comprimés / blister ×

blisters / box ×
blisters / boîte ×

boxes / ctn
boîtes / ctn

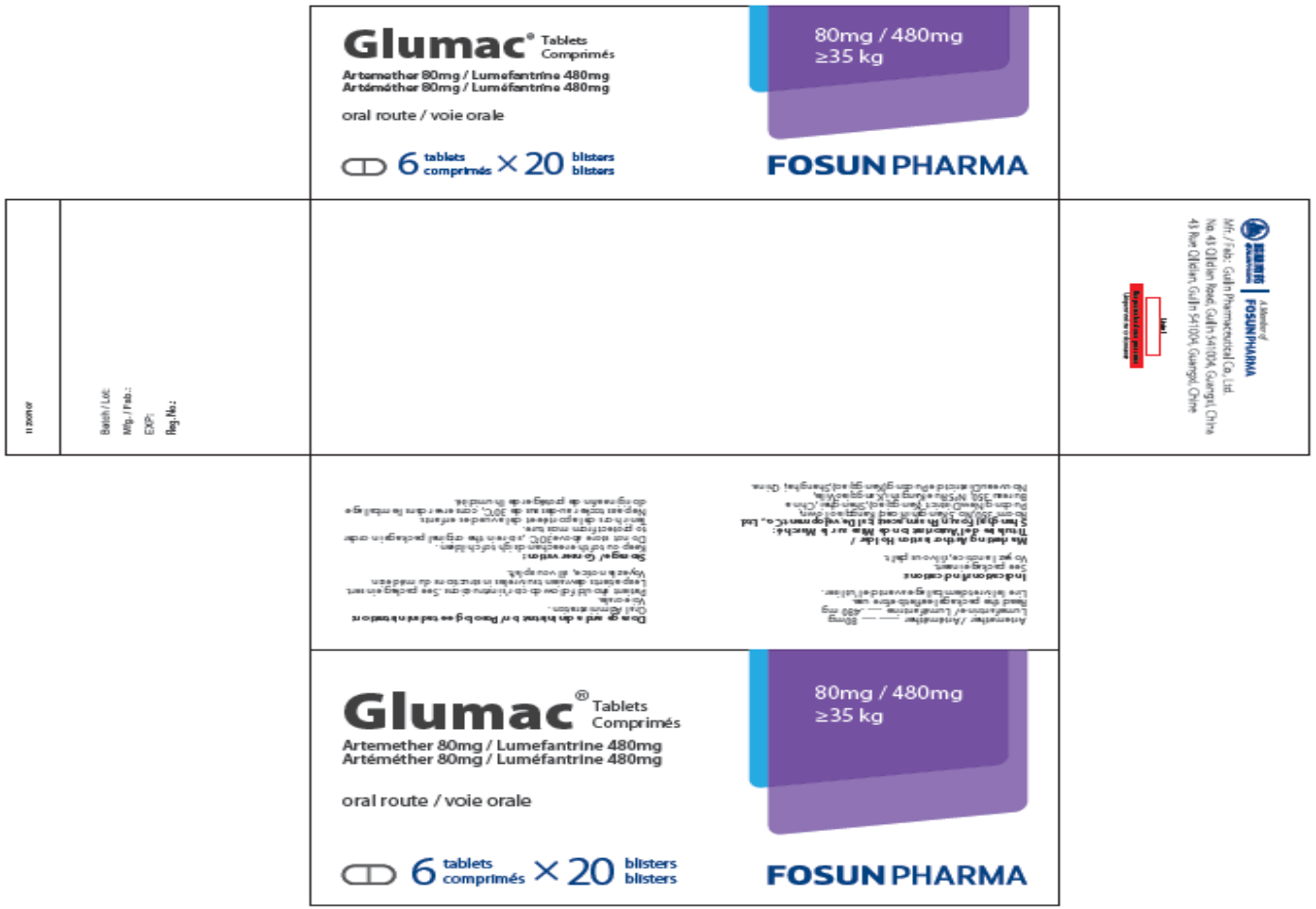
112007405

Liste I

Respecter les doses prescrites
Uniquement sur ordonnance

Made in China

Effective date: 03/10/2022



Effective date: 03/10/2022