

TMDA/DMC/MRE/F/016

Rev #:02

THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

**PUBLIC ASSESSMENT REPORT FOR FIRIALTA (FINERENONE 10 MG) FILM
COATED TABLETS**

Version number 01, 06/01/2023

**TMDA Headquarters, Plot No. 56/1, Block E, Kisasa B Centre, Swaswa Road,
P. O. Box 1253, Dodoma – Tanzania, Telephone: +255 (26)
2961989/2061990/+255 (22) 2450512/2450751/2452108, Email:
info@tmda.go.tz, Website: www.tmda.go.tz
Toll free: 0800110084**

1. Introduction

Finerenone is a nonsteroidal, selective antagonist of the mineralocorticoid receptor (MR) which is activated by aldosterone and cortisol and regulates gene transcription. Its binding to the MR leads to a specific receptor-ligand complex that blocks recruitment of transcriptional coactivators implicated in the expression of pro-inflammatory and pro-fibrotic mediators.

Finerenone is approved in Tanzania for the treatment of chronic kidney disease (stage 3 and 4 with albuminuria) associated with type 2 diabetes in adults.

1.1.Product details

Registration number	TAN 22 HM 0510
Brand name	Firialta 10 mg film-coated tablets
Generic name, strength and form	Finerenone
ATC classification	Diuretics, aldosterone antagonists, ATC code: C03DA05
Distribution category	POM
Country of origin	Germany
Associated product	The finished product is presented as a film-coated tablet containing 10 mg or 20 mg of Finerenone as active substance
Marketing Authorization Holder	Bayer AG , 51368 Leverkusen Germany
Local Technical Representative	JD Pharmacy Limited, Dar Es Salaam, Tanzania

1.2.Assessment procedure

The application for registration of Firialta 10 mg film-coated tablets was submitted on 20/06/2022. The product underwent abridged assessment. Assessment was completed in one round of evaluation. Firialta 10 mg film-coated tablets was registered on 05/12/2022.

1.3.Information for users

Visual description of the finished product	pink film-coated, oval oblong tablet with a length of 10 mm, a width of 5 mm, a radius of curvature of 3.4 mm, a height of 3.1 – 3.7 mm and a weight of 136.00 mg. The tablets are marked with “10” on the top side and “FI” on the bottom side
Primary packing material	Pack of 2 x 14's film coated tablets in PVC/PVDC/Aluminium blister pack
Secondary packing materials	Carton box alongside with a package insert
Shelf-life and storage condition	36 months Do not store above 30°C
Route of administration	Oral
Therapeutic indications	Firialta 10 mg film-coated tablets is indicated for the treatment of chronic kidney disease (stage 3 and 4 with albuminuria) associated with type 2 diabetes in adults.

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 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: Firialta 10 mg film-coated tablets

Composition: Each film-coated tablet contains 10 mg of Finerenone

Pack size: 2 x 14's tablets

Manufacturing details: batch number, manufacturing date, expiry date

Storage conditions: Do not store above 30°C

Manufacturer address: Bayer AG, Kaiser-Wilhelm-Allee, 51368 Leverkusen Germany

Unique identifier: N/A

Special warnings/precautions or instructions for use: This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

The details of the primary pack include:

Brand name and strength: Firalta 10 mg film-coated tablets

Manufacturing details: batch number, manufacturing date, expiry date

Name of manufacturer: Bayer AG, Kaiser-Wilhelm-Allee, 51368 Leverkusen Germany.

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)

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

General properties

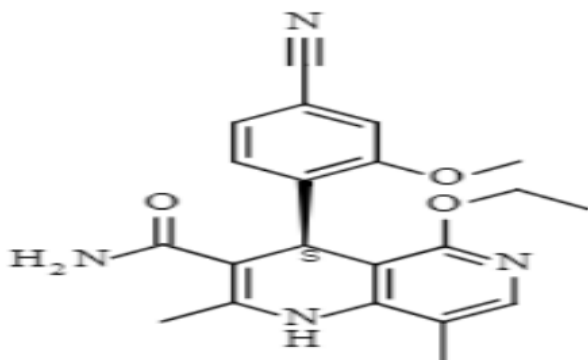
Finerenone API is non-compensated.

Molecular formula: $C_{21}H_{22}N_4O_3$

Chemical names:

(4S)-4-(4-cyano-2-methoxyphenyl)-5-ethoxy-2,8-dimethyl-1,4-dihydro-1,6-naphthyridine-3-carboxamide

Structure:



Critical physico-chemical properties are:

The active substance is a white to yellow crystalline non-hygroscopic powder. It is soluble in methanol and sparingly soluble in ethanol, acetonitrile and acetone. Its solubility in aqueous media is strongly pH- dependent, being soluble at pH 1 and practically insoluble at pH above 4.5.

Finerenone has one stereocentre with S configuration. Enantiomeric purity is controlled routinely by chiral HPLC.

Manufacture

The API manufacturing site;

Step	Site
Synthesis of finerenone	Bayer AG, Wuppertal AMPAC Fine Chemicals, Rancho Cordova ^a
Micronization	Bayer AG, Leverkusen Bayer AG, Berlin
Packaging	Bayer AG, Leverkusen Bayer AG, Berlin
Quality control testing	Bayer AG, Wuppertal Bayer AG, Bergkamen Bayer AG, Leverkusen

The manufacturing facilities were noted to comply with WHO GMP requirements as evidenced by the GMP certificate issued by ___ Local administrative district (Bezirksregierung) of Düsseldorf , Germany _____. Finerenone 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 in-house standards and ICHQ3A. The parameters monitored during quality control are: appearance and colour, identity (IR, HPLC), PSD (laser diffraction), enantiomeric purity (RP-HPLC), water content (KF), residual solvents (HS-GC), related substances (RP-HPLC) and assay (RP-HPLC). Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The stability results indicate that the active substance made by the proposed manufacturers is sufficiently stable. The stability results justify the proposed retest period of 24 months in the proposed container which has been demonstrated.

Quality of the Finished Pharmaceutical Product

Formulation

Firialta 10 mg film-coated tablets is presented as pink film-coated, oval oblong tablet with a length of 10 mm, a width of 5 mm, a radius of curvature of 3.4 mm, a height of 3.1 – 3.7 mm and a weight of 136.00 mg. The tablets are marked with “10” on the top side and “FI” on the bottom side.

Firialta 10 mg film-coated tablets contains Finerenone and other ingredients listed here after: Cellulose, microcrystalline, Croscarmellose sodium, Hypromellose 2910, Lactose monohydrate, Magnesium stearate, Sodium laurilsulfate. The quantities of all ingredients are confirmed to be in line with the recommendations of Handbook of Pharmaceutical Excipients, Edition 8th in terms of function and quantities. Ingredient, lactose is of safety concern therefore appropriate warnings were included in the product label.

Film coat: Hypromellose 2910, Titanium dioxide, Talc and Iron oxide red

Manufacture

The finished product was manufactured at Bayer AG, Kaiser-Wilhelm-Allee, 51368 Leverkusen Germany. The compliance of the site to TMDA GMP standards was confirmed through desk review.

Specifications

The FPP is non-compensated. The manufacturer controls the quality of the finished product as per in-house standards and ICH requirements. The parameters monitored during quality control are: appearance, identity (HPLC/UPLC, retention time and UV

spectrum), uniformity of dosage units (Ph. Eur), dissolution (Ph. Eur), degradation products (HPLC/UPLC), assay (HPLC/UPLC), microbial purity, TAMC, TYMC and E. coli (Ph. Eur.). 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 $30 \pm 2^\circ\text{C}$ & $75\% \pm 5\%$ RH for 36 months and $40 \pm 2^\circ\text{C}$ & $75\% \pm 5\%$ RH for 6 months. Based on available stability data, the proposed shelf-life of 36 months is acceptable.

Safety and efficacy information

TMDA has not assessed the primary data relating to preclinical and clinical aspects of this application and is taking over the results of the assessment of the foreign reference authority of EMA. The current TMDAPAR relating to preclinical and clinical aspects refers to the publicly available Assessment Report for Firalta 10 mg film-coated tablets / Kerendia issued by the EMA through Procedure No. EMEA/H/C/005200/0000.

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 Firalta 10 mg film-coated tablets is recommended for registration.

5. Post-approval updates

Variation applications

Reference number	D a t e 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

Versio n	Date	Description of update	S e c t i o n (s) Modified	A p p r o v a l date

Annex I: Mock up label

