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**MINISTRYOFHEALTH**

**TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY**

# PUBLIC ASSESSMENT REPORT FOR FIRIALTA (FINERENONE 20 MG) FILM COATED TABLETS

**Version number 01, 06/01/2023**

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## 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 0511 |
| Brand name | Firialta 20 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,<br>Dar Es Salaam, Tanzania |

### 1.2.Assessment procedure

The application for registration of Firialta 20 mg film-coated tablets was submitted on 20/07/2022. The product underwent abridged EAC joint assessment. Assessment was completed in one round of evaluation. Firialta 20 mg film-coated tablets was registered on 05/12/2022.

### 1.3.Information for users

| | |
|---|---|
| Visual description of the finished product | Pale-yellow 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 “20” 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<br>Do not store above 30°C |
| Route of administration | Oral |
| Therapeutic indications | Firialta 20 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 20 mg film-coated tablets

Composition: Each film-coated tablet contains 20 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: Firialta 20 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)

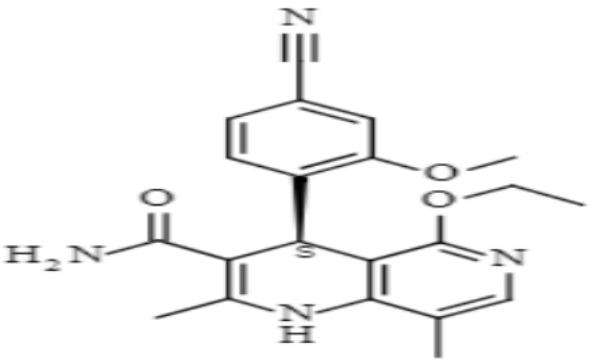
Information on quality of the API was submitted in form of full details.

General properties
Finerenone API is non-compendia.

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<br>AMPAC Fine Chemicals, Rancho Cordova [a] |
| Micronization | Bayer AG, Leverkusen<br>Bayer AG, Berlin |
| Packaging | Bayer AG, Leverkusen<br>Bayer AG, Berlin |
| Quality control testing | Bayer AG, Wuppertal<br>Bayer AG, Bergkamen<br>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 20 mg film-coated tablets is presented as pale-yellow 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 “20” on the top side and “FI” on the bottom side.

Firialta 20 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 8$^{th}$ 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 yellow

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-compendia. 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 ± 2°C & 75% ± 5% RH for 36 months and 40 ± 2°C & 75% ± 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 Firialta 20 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 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 Firialta 20 mg film-coated tablets 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 | Date | Description of update | Section(s) Modified | Approval date |
|---|---|---|---|---|
| | | | | |

Annex I: Mock up label