THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR OLEPTISS 90 (DEFERASIROX 90 MG) FILM COATED TABLETS

Version number 1.0
21 August, 2023

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1. Introduction

OLEPTISS 90 tablets is a generic medicinal version of “Exjade tablets” by Novartis Europharm Limited contains Deferasirox 90 mg per each tablet. Deferasirox is an orally active chelator that is highly selective for iron (III). It is a tridentate ligand that binds iron with high affinity in a 2:1 ratio. Deferasirox promotes excretion of iron, primarily in the feces. Deferasirox has low affinity for zinc and copper, and does not cause constant low serum levels of these metals. OLEPTISS 90 tablets is approved in Tanzania for use in adult and paediatric patients aged 2 years and older

Product details

Registration number	TAN 23 HM 0272
Brand name	OLEPTISS 90
Generic name, strength, and form	Each film-coated tablet contains 90 mg Deferasirox
ATC classification	A10BD07 - Medicines used in diabetes, Dipeptidyl peptidase 4 (DPP-4) inhibitors
Distribution category	POM
Country of origin	India
Associated product	OLEPTISS 360
Marketing Authorization Holder	NVS Kenya Limited-on behalf of MAH-Novartis Overseas Investment Britam Tower, 27th Floor, Hospital Road, Upper Hill P.O. Box 46057 00100, Nairobi Kenya
Local Technical Representative	JD Pharmacy Limited P.O. Box 1899 Dar es Salaam, Tanzania

1.1 Assessment procedure

The application for registration of OLEPTISS 90 film coated tablet was submitted in 12/08/2022. The product underwent abridged assessment. Assessment was completed in 1 (one) rounds of evaluation and the product was registered on 01/06/2023.

1.2 Information for users

Visual description of the finished product	Light blue unscored ovaloid biconvex film-coated tablet with beveled edges, debossed with ‘NVR’ on one side and ‘90’ on a slight upward slope in between two debossed curved lines on the other side. Dimensions: Approx. 10.7 x 4.2 mm
Primary packing material	PVC/PVDC/Aluminium blister
Secondary packing materials	Printed carton box
Shelf-life and storage condition	24 months, Do not above 30°C. Protect from moisture.
Route of administration	Oral

Therapeutic indications	Oleptiss is indicated for the treatment of chronic iron overload due to blood transfusions (transfusional hemosiderosis) in adult and pediatric patients (aged 2 years and over). Oleptiss is also indicated for the treatment of chronic iron overload in patients with non-transfusion-dependent thalassemia syndromes aged 10 years and older.

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: OLEPTISS 90

Composition: Each film-coated tablet contains 90 mg Deferasirox

Pack size: 30 tablets

Manufacturing details: batch number, manufacturing date, and expiry date

Storage conditions: Do not above 30°C. Protect from moisture.

Manufacturer address: physical address of release site

Unique identifier: Not applicable

Special warnings/precautions or instructions for use: N/A

The details of the primary pack include:

Brand name and strength: N/A

Manufacturing details: batch number, manufacturing date and expiry date

Name of manufacturer: SANDOZ S.R.L

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

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

General Information

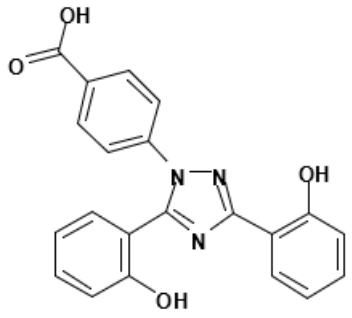
Deferasirox API is compendia in Ph.Eur./BP.

Molecular formula: $C_{21}H_{15}N_3O_4$

Chemical name:

4-[3,5-Bis(2-hydroxyphenyl)-[1,2,4]-triazol-1-yl] benzoic acid

Structure:



General properties

The active substance is deferasirox, an established active substance for which no monograph is available yet. The active substance is a crystalline white powder, is soluble in DMSO and DMF and not soluble in water. Deferasirox has no chiral centres and is not optically active. Deferasirox has two polymorphic forms; the substance used in drug product at issue is pure form A.

Deferasirox is reported to be a BCS Class II drug substance (poorly soluble, highly permeable drug). Hence particle size and distribution and polymorphism are controlled in the API specifications since are considered to be critical.

Manufacture

Deferasirox API manufacturer is Novartis Pharma AG, Lichtstrasse 35, 4056 Basel, Switzerland, Novartis Pharma Schweizerhalle AG, Rothausstrasse, 4133 Pratteln, Switzerland, and Novartis Pharma Stein AG, Schaffhauserstrasse, 4332 Stein, Switzerland, SK Biotek Co., Ltd, 80 Myeonghaksandan-Ro, Yeondong-Myeon, Sejong-si, 30068, Korea, South. The manufacturing complies with GMP requirements as evidenced by the GMP certificate issued by <state the issuing authority>. Deferasirox 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

Specifications

The API specifications were set as per USP, in-house standards and ICHQ3A. The parameters monitored during quality control are: appearance by visual determination, identity by IR spectroscopy and X-ray diffraction pattern, water by Karl Fischer titration, sulfated ash, heavy metals by ICP-OES/ICP-MS, clarity of solution, colour of solution, and microbial enumeration tests. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The retest period of Deferasirox API is 36 months when packed in double lined polyethylene bags with storage condition ‘Do not store above 30°C’

Quality of the Finished Pharmaceutical Product

Formulation

OLEPTISS 90 film coated tablet is a light blue unscored ovaloid biconvex film-coated tablet with beveled edges, debossed with ‘NVR’ on one side and ‘90’ on a slight upward slope in between two debossed curved lines on the other side. Dimensions: Approx. 10.7 x 4.2 mm

OLEPTISS 90 film coated tablet contains the Deferasirox and other ingredients listed here after: Microcrystalline cellulose; crospovidone; povidone (K30); magnesium stearate; colloidal silicon dioxide; poloxamer 188; coating material: hypromellose; titanium dioxide (E171); polyethylene glycol (4000); talc; FD&C blue #2/Indigo carminine aluminum lake (E132). The quantities of all ingredients are confirmed to be in line with the recommendations of Handbook of Pharmaceutical Excipients, 8th Edition in terms of function and quantities.

Manufacture

The finished product manufacturers are Novartis Pharma Stein AG, Schaffhauserstrasse, 4332 Stein, Switzerland, Novartis Pharma Productions GmbH, Öflinger Strasse 44, 79664 Wehr, Germany and Sandoz S. R.L., 7A Livezeni Street, Targu Mures, 540472, Romania (ROU). The compliance of the sites to TMDA GMP standards was confirmed through site inspection on DD/MM/YYYY.

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 by NIR and UV, identity of colorants by color reaction (titanium, iron, and ndigotine), Mean mass, assay and determination of degradation products by HPLC, dissolution by HPLC, assay and uniformity of dosage units by NIR, uniformity of dosage units by content uniformity by HPLC, degradation products, microbial enumeration. 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 ± 2°C & RH: 75 ± 5% RH for 24 months and 40± 2°C & RH: 75% ± 5% RH for 6 months. Based on the stability data presented, the approved shelf-life is 24 months when stored in PVC/PVDC/Aluminium blister with storage condition ‘Do not store above 30°C. Protect moisture’.

Safety and efficacy information

OLEPTISS 90 film-coated tablets are already registered by countries with stringent regulatory authorities, namely Switzerland and Romania. Information on clinical data has been fully evaluated during the registration of the product by the competent authorities in the mentioned countries. In this context, a re-assessment of this part is not considered as necessary.

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. OLEPTISS 90 film coated tablet 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>.

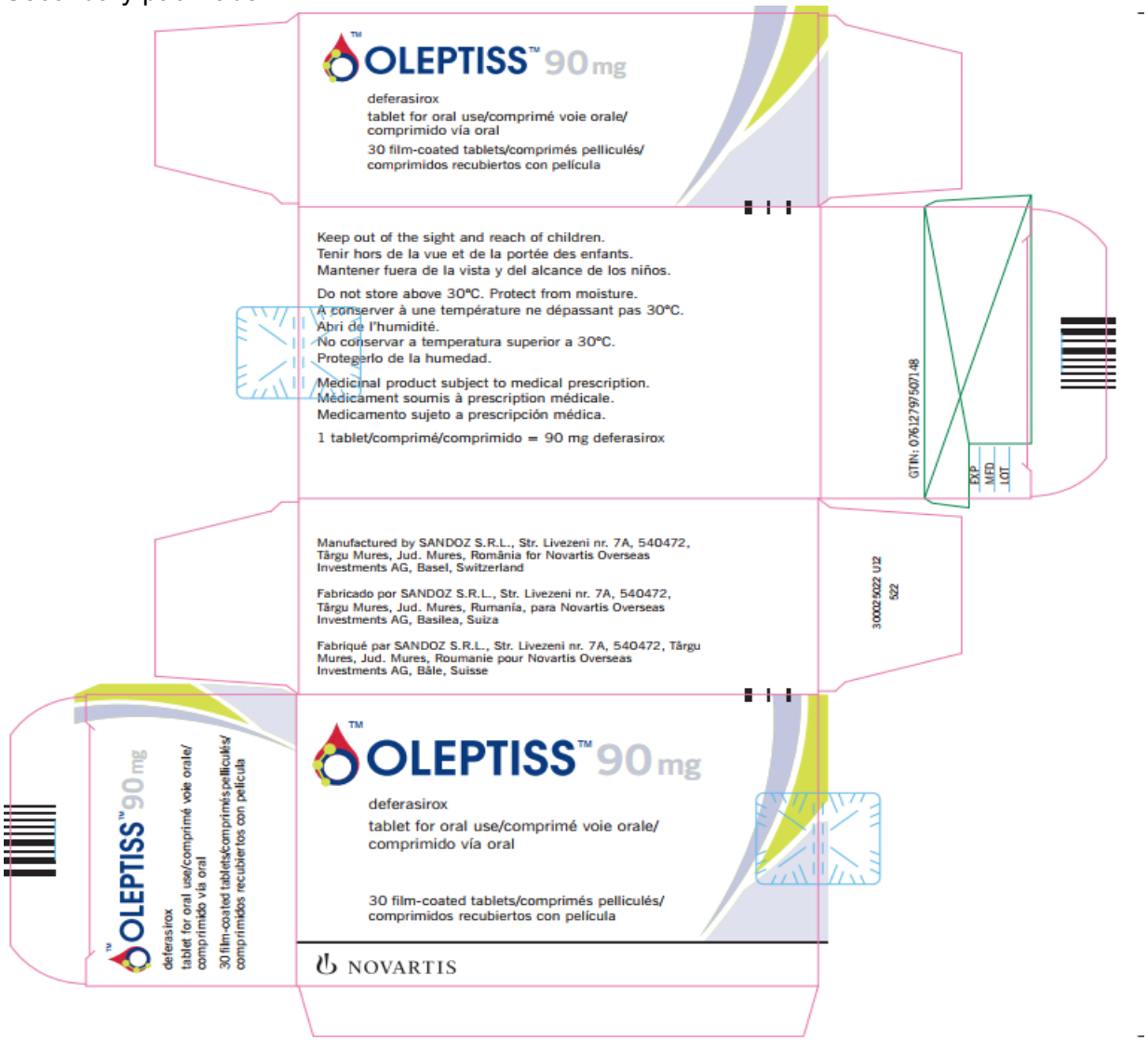
PART 5: CHANGE HISTORY

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

Annex I: Mock up labels;

Primary pack label;

Secondary pack label:



Effective date: 03/10/2022