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MINISTRYOFHEALTH

TANZANIA MEDICINES AND MEDICALDEVICES AUTHORITY

# PUBLIC ASSESSMENT REPORT FOR VIVAZAC 300 (IRBESARTAN 300 MG ) AND VIVAZAC 150 ( IRBESARTAN 150 MG )TABLETS

**Version number 1.0**
**11 October 2023**

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## 1. Introduction

Vivazac is a generic medicine of irbesartan tablets. Vivazac is a an antihypertensive medicine belonging to C09C A04- Angiotensin-II antagonists, plain group. Vivazac exerts is activity by selectively blocking angiotensin-II receptor (type AT1) resulting to an increase in plasma renin levels and angiotensin-II levels, and a decrease in plasma aldosterone concentration.Vivazac is approved in Tanzania for use in <adults, children, elderly etc>.

### 1.1 Product details

| | |
|---|---|
| Registration number | Vivazac 300: TAN 20 HM 0352<br>Vivazac 150: TAN 20 HM 0405 |
| Brand name | Vivazac 300 mg tablets<br>Vivazac 150 mg tablets |
| Generic name, strength and form | Irbesartan 300 mg tablets<br>Irbesartan 150 mg tablets |
| ATC classification | C09C A04- Angiotensin-II antagonists, plain |
| Distribution category | POM |
| Country of origin | Jordan |
| Associated product | NA |
| Marketing Authorization Holder | United Pharmaceuticals Manufacturing Limited Company,<br>Al-Rageem- Sahab<br>Amman**-Jordan**<br>E-Mail: samar.amaireh@mspharma.com |
| Local Technical Representative | Wide Spectrum (T) Limited,<br>Sukuku Street Kariakoo,<br>P.O. Box: 90518,<br>Dar Es Salaam**-Tanzania** |

### 1.2 Assessment procedure

The application for registration of Vivazac 300 mg tablets/ Vivazac 150 mg tablets was submitted on <DDMMYYYY>. The product underwent full assessment. Assessment was completed in 5 rounds of evaluation. Vivazac 300 mg tablets and Vivazac 150 were registered on 25/09/2020.

### 1.3 Information for users

| | |
|---|---|
| Visual description of the finished product | Vivazac 300: White biconvex caplet shape tablet embossed with E41 on one side and plane on the other<br>Vivazac 150: White biconvex oval shaped tablet |

| | |
|---|---|
| | embossed with E40 on one side and plane on the other |
| Primary packing material | PVC/PVDC/Al |
| Secondary packing materials | |
| Shelf-life and storage condition | 24 months<br>Store up to 30°C, protect from moisture |
| Route of administration | Oral |
| Therapeutic indications | Indicated in adults for the treatment of essential hypertension. It is also indicated for the treatment of renal disease in adult patients with hypertension and type 2 diabetes mellitus as part of an antihypertensive medicinal product 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 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: Vivazac 300, Vivazac 150
Composition: Irbesartan 300 mg tablets, Irbesartan 150 mg tablets
Pack size: 3 × 10 tablets
Manufacturing details: batch number, manufacturing date, expiry date
Storage conditions: Store up to 30°C, protect from moisture.
Manufacturer address: United Pharmaceuticals Manufacturing Limited Company, Al-Rageem-Sahab, Amman-Jordan

Unique identifier: <state the unique identification used>

Special warnings/precautions or instructions for use: The product contains lactose

The details of the primary pack include:
Brand name and strength: Vivazac 300, Vivazac 150
Manufacturing details: <batch number, manufacturing date, expiry date>
Name of manufacturer: United Pharmaceuticals

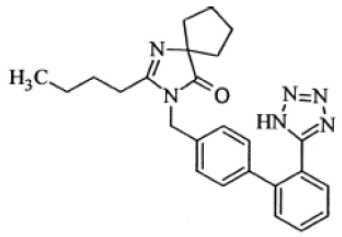
The content of the primary and secondary labels was aligned to the requirements of the Part V of the Compendium: Guidelines on Format and Content of Product Labels for Medicinal products. The label contains sufficient information for proper identification of the medicine and post marketing follow up of the product.
Describe any approved deviation to the requirements and the justification for the deviation.

## 3. Scientific discussion

### Quality of Active Pharmaceutical Ingredient(s)

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

General properties
Irbesartan API is compendia in BP.
Molecular formula: $C_{25}H_{28}N_6O$
Chemical name: 1,3-Diazaspiro[4.4]non-1-en-4-one,2-butyl-3-[[2'-(1H-tetrazol-5-yl)[1,1'- biphenyl]-4-yl]-methyl]-
Structure:



Critical physico-chemical properties of the API were sparingly soluble in Methanol, slightly soluble in Methylene Chloride and practically insoluble in Water.It exhibits polymorphism and form-A is manufactured.

Manufacture
The API manufacturing site, Jubilant Generics Limited/ #18,56,57 & 58, K.I.A.D.B Industrial area, Nanjangud, Mysore District 571 302 Karnataka, India was noted to comply with WHO GMP requirements as evidenced by the GMP certificate issued by Government of Karnataka Drugs Control Department. Irbesartan 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 Ph.Eur standards and ICHQ3A. The parameters monitored during quality control are: characters,solubility, identification , appearance of solution, water content, heavy metals, sulphated ash, limit of azide (trinitride): N3- ( Impurity B),

related substances,assay, residual sovents,particle size, content of NDMA impurity and content of NDEA impurity .Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The re-test period of Irbesartan API is 48 months when packed in polyethylene bag and stored at below 25ºC.

**Quality of the Finished Pharmaceutical Product**

Formulation

Vivazac 300 is a white biconvex caplet shape tablet embossed with E41 on one side and plane on the other. Vivazac 150 is a white biconvex oval shaped tablet embossed with E40 on one side and plane on the other. Vivazac contains Irbesartan and other ingredients listed hereafter lactose monohydrate, croscarmellose sodium, hypromellose, microcrystalline cellulose, colloidal silicon dioxide, magnesium stearate and HPMC based coating system.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 monohydrate is of safety concern therefore appropriate warnings were included in the product label.

Manufacture

The finished product was manufactured at United Pharmaceuticals Manufacturing Limited Company, Al-Rageem- Sahab, Amman-Jordan. The compliance of the site to TMDA GMP standards was confirmed through site inspection on 3$^{rd}$ & 4$^{th}$ October, 2018.

Specifications

The FPP is compendial in USP. The manufacturer controls the quality of the finished product as per USP and ICHQ3B requirements. The parameters monitored during quality control are: description, identification, average weight, weight variation, uniformity of dosage units, disintegration, dissolution, related substances, assay and microbial limit test.Compliance to the standard was established using batch analysis data and stability data.

Stability and container closure system

Stability studies were conducted on 3 batches of the finished product stored at 30°C ± 2°C, 65 % ± 5 % for 24 months and 40°C ± 2°C, 75 % ± 5 % for 6 months. Based on the stability data presented, the approved shelf-life is 24 months when stored in PVC/PVDC/Al blisters at below 30ºC.

**Safety and efficacy information**

**Vivazac 300 tablets**

Safety and efficacy of Vivazac 300 was established through bioequivalence trial. BE trial report number <number> was submitted.

| | | |
|---|---|---|
| Study title | A comparative bioavailability study which include fasting bioequivalence study of IRBESARTAN TABLETS 300 mg by UNITED PHARMACEUTICALS MFG CO. VERSUS APROVEL TABLETS 300 mg SANOFI WINTHROP INDUSTRIES innovator product following a single dose administration of one tablet to healthy adults under fasting condition | |
| Study design | This study was an open label randomized fasting single dose two treatment two sequence two period crossover laboratory blind studies with a washout interval of one week between dosing | |
| Study site | Akleh Hospital,<br>Jabal Amman, 3rd Circle,<br>P.O. Box: 831201,<br>Amman 11183,<br>**JORDAN.** | |
| Study dates | 16/03/2011 - 13/04/2011 (Clinical and bioanalytical phase) | |
| Primary objective | | |
| Secondary objective | | |
| Number of participants | 28 | |
| Monitored parameters | Cmax, AUCt, AUCinf | |
| Investigational medicinal products | Test Product<br>Irbesartan tablets of United Pharmaceuticals Mfg Co | Reference product<br>Aprovel Tablets of Sanofi Winthrop Industrie |
| | Strength: 300 mg<br>Batch number: 7941<br>Expiry date: 12/2012 | Strength: 300 mg<br>Batch number:2854<br>Expiry date: 02/2012 |
| Analytical method | HPLC-MS/MS | |
| Statistical method | | |

Efficacy results are summarized as follows:

| Parameter | Test | Reference | % Ratio of geometric means | 90 % Confidence interval | DF | CV (%) |
|---|---|---|---|---|---|---|
| AUC0-t (µg x hr/ml) | 20.030±8.558 | 21.110±8.920 | 96.76 | | | |
| AUC0-inf (µg x hr/ml) | 23.030±8.833 | 22.824±8.920 | 98.24 | | | |
| Cmax (µg/ml) | 4.121±1.368 | 3.934±1.215 | 104.00 | | | |

The acceptance limits of 80 – 125% are met by the AUC and Cmax values. Furthermore, the safety profile of the test product is similar to that of reference product. Therefore, Vivazac 300 is equivalent and interchangeable with Aprovel Tablets under acceptable in vivo experimental conditions.

**Vivazac 150 tablets**

Safety and efficacy of Vivazac 150 was established through biowaiver application. Comparative dissolution report number <number> was submitted.

The biowaiver was approved based on additional strength.

Vivazac 150 fulfilled the criteriafor waiving an in-vivo bioequivalence study as per relevant TMDA guidance. Dissolution profiles of Vivazac 150 tablets was compared to Vivazac 300 mg tablets. Less than> 85% of the labelled amount of irbesartan had dissolved in all three media. Therefore, necessitating calculation of similarity factor f2, which was noted to be above 50.

## 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. <Brand name> 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 label

**Vivazac 300**


Each film coated tablet contains: Irbesartan 300 mg.
This product contain lactose
Indications and Dosage: See enclosed leaflet.
Store up to 30°C, protect from moisture.
Keep out of the reach of children.
To be dispensed on medical prescription.
United Pharmaceuticals Manufacturing Limited company,
Al-Rageem -Sahab, Amman-Jordan.
كل قرص مغلف يحتوي على: اربيسارتان ٣٠٠ ملغم.
هذا المنتج يحتوي على لاكتوز.
الإستعمال والجرعات: أنظر النشرة المرفقة.
يحفظ حتى ٣٠°م، بعيداً عن الرطوبة.
يحفظ بعيداً عن متناول الأطفال.
يصرف بوصفة طبية.
الشركه المتحده لصناعة الأدويه ذ.م.م. الرجيب –سحاب– عمان– الأردن.
Batch No.:
Mfg. Date:
Exp. Date:
M3x11-1850
M3x11-1850
M3x11-1850
فيفيزاك®
اربيسارتان
٣٠٠ ملغم
٣*١٠ قرص مغلف
2623
152
black
United Pharmaceuticals
Vivazac®
Irbesartan
300 mg
3*10 Film Coated Tablets
Vivazac® Irbesartan 300 mg
86x69x30 mm
6 251653 260103

**Vivazac 150**


Vazac
irbesartan
150 mg
United
Pharmaceuticals
M3×10×0426


Effective date: 03/10/2022