THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR DERMAZOLE (KETOCONAZOLE 2%W/W) CREAM

Version number 1.0
21 August, 2023

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1. Introduction

Dermazole Cream is a white homogenous cream containing the 20 mg Ketoconazole per each gram of cream. The reference product is Nizoral 2% Cream of Janssen-Cilag Ltd. Ketoconazole, a synthetic imidazole dioxolane derivative, has a potent antimycotic activity against dermatophytes such as Trichophyton spp., Epidermophyton floccosum and Microsporum spp. and against yeasts, including Malassezia spp. and Candida spp. The effect on Malassezia spp. is particularly pronounced. Dermazole Cream is approved in Tanzania for use in all ages.

Product details

Registration number	TAN 23 HM 0275
Brand name	Dermazole
Generic name, strength, and form	Each gram of cream contains: Ketoconazole…… 20 mg
ATC classification	ATC Code - D01AC08 – Antifungals for Topical Use, Imidazole and triazole derivatives
Distribution category	POM
Country of origin	India
Associated product	N/A
Marketing Authorization Holder	Kusum Healthcare Pvt. Ltd. D-158A, Okhla Industrial Area, Phase 1, New Delhi – 110020, India
Local Technical Representative	RK Pharmaceuticals (Tanzania) limited Plot No. 9, Block No. 28, Uhuru/Swahili, Dar Es Salaam, Tanzania

1.1 Assessment procedure

The application for registration of Dermazole was submitted on DD/MM/YYYY. The product underwent full assessment. Assessment was completed in 2 (two) rounds of evaluation and the product was registered on 01/06/2023.

1.2 Information for users

Visual description of the finished product	White homogenous cream
Primary packing material	Aluminium tube
Secondary packing materials	Carton
Shelf-life and storage condition	36 months, Do not store above 30°C. Do not freeze.
Route of administration	Topical application
Therapeutic indications	For topical application in the treatment of dermatophyte infections of the skin such as tinea corporis, tinea cruris, tinea manus and tinea pedis infections due to Trichophyton spp, Microsporon

	spp and Epidermophyton spp. Dermazole 2% cream is also indicated for the treatment of cutaneous candidosis (including vulvitis), tinea (pityriasis) versicolor and seborrhoeic dermatitis caused by Malassezia (previously called Pityrosporum) spp

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: Dermazole

Composition: Each gram of cream contains Ketoconazole…… 20 mg, Propylene glycol, Cetostearyl alcohol, Cetomacrogol 1000, White soft paraffin, Light liquid paraffin, Disodium edetate, Sodium sulfite anhydrous, Polysorbate-80 & Purified water

Pack size: 15 gram

Manufacturing details: batch number, manufacturing date, expiry date

Storage conditions: Do not store above 30°C. Do not freeze.

Manufacturer address: physical address of release site

Unique identifier:

Special warnings/precautions or instructions for use:

The details of the primary pack include:

Brand name and strength: Not applicable

Manufacturing details: batch number, manufacturing date and expiry date

Name of manufacturer: Kusum Healthcare Pvt. 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

A. <u>Ketoconazole from AARTI Drugs Limited:</u>

General Information

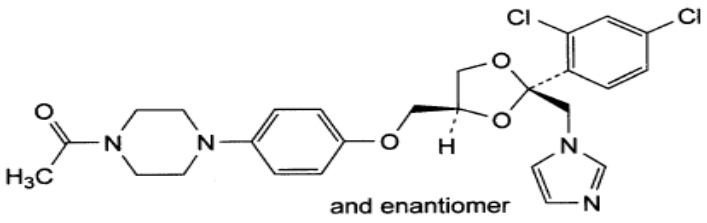
Ketoconazole API is compendia in USP, BP, and Ph.Eur.

Molecular formula: $C_{26}H_{28}Cl_2N_4O_4$

Chemical name:

1-acetyl-4-[4-[[(2RS,4SR)-2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl] methoxy] phenyl] piperazine, or (±)-cis-1-Acetyl-4-(p-[[2-(2,4-dichlorophenyl)-2-(imidazol-1-ylmethyl)-1,3-dioxolan-4-yl] methoxy] phenyl) piperazine

Structure:



General properties

Ketoconazole is a white or almost white powder, practically insoluble in water, freely soluble in methylene chloride, soluble in methanol and sparingly soluble in ethanol (96%). The molecule has two chiral centres. The form produced is optically inactive.

Manufacture

Ketoconazole API manufacturer is AARTI Drugs Limited, Plot No. E – 21, M.I.D.C., Tarapur, Tal. – Palghar, Dist.: Palghar- 401 506, Maharashtra, India.The manufacturing complies with

GMP requirements as evidenced by the GMP certificate issued by the Food and Drugs Administration, Maharashtra. Ketoconazole 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 USP standards and ICHQ3A. The parameters monitored during quality control are: Description, Solubility, Identification by IR and HPLC, Specific Rotation, Loss on drying, Organic Impurities, Assay, Residual solvents, Particle size, Extraneous Matter, Microbial limit tests. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The re-test period of Ketoconazole API is 60 months when packed in double polythene bag in sealed fiber drums with storage condition 'Store at room temperature'.

B. Ketoconazole from Sharon Bio-Medicine Ltd

General Information

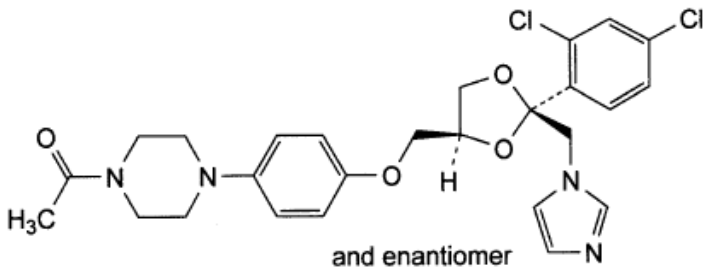
Ketoconazole API is compendia in USP, BP, and Ph.Eur.

Molecular formula: $C_{26}H_{28}Cl_2N_4O_4$

Chemical name:

1-acetyl-4-[4-[[(2RS,4SR)-2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl] methoxy] phenyl] piperazine, or (±)-cis-1-Acetyl-4-(p-[[2-(2,4-dichlorophenyl)-2-(imidazol-1-ylmethyl)-1,3-dioxolan-4-yl] methoxy] phenyl) piperazine

Structure:



General properties

Ketoconazole is a white or almost white powder, practically insoluble in water, freely soluble in methylene chloride, soluble in methanol and sparingly soluble in ethanol (96%). The molecule has two chiral centres. The form produced is optically inactive.

Manufacture

Ketoconazole API manufacturer is Sharon Bio-Medicine Ltd, Plot No. L-6, MIDC, Taloja, Raigad – Dist, Maharashtra – 410208, India.The manufacturing complies with GMP requirements as evidenced by the GMP certificate issued by the Food and Drugs Administration, Maharashtra. Ketoconazole 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 USP standards and ICHQ3A. The parameters monitored during quality control are: Description, Solubility, Identification by IR and HPLC, Specific Rotation, Loss on drying, Organic Impurities, Assay, Residual solvents, Particle size, Extraneous Matter, Microbial limit tests. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The re-test period of Ketoconazole API is 60 months when packed in double polythene bag in sealed fiber drums with storage condition ‘Store at room temperature’.

Quality of the Finished Pharmaceutical Product

Formulation

Dermazole is a white homogeneous cream.

Dermazole contains the Ketoconazole other ingredients listed here after: Propylene glycol, Cetostearyl alcohol, Cetomacrogol 1000, White soft paraffin, Light liquid paraffin, Disodium edetate, Sodium sulfite anhydrous, Polysorbate-80 & Purified water. 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 Kusum Healthcare Pvt. Ltd, SP-289 (A), RIICO Industrial Area, Chopanki, Bhiwadi, Dist. Alwar, Rajasthan. The compliance of the sites to TMDA GMP standards was confirmed through site inspection on DD/MM/YYYY.

Specifications

The FPP is compendia. The manufacturer controls the quality of the finished product as per USP standards and ICH requirements. The parameters monitored during quality control are: Description, Identification of API, (by HPLC and TLC), Identification of Sodium Sulfite (by HPLC), Homogeneity & Phase separation, pH, Minimum fill, Viscosity, Related Substance, Assay of API, Assay of Sodium Sulfite, and Microbial Purity. 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 36 months and 40± 2°C & RH: 75% ± 5% RH for 6 months. Based on the stability data presented, the approved shelf-life is 36 months when stored in Aluminium tube with storage condition 'Do not store above 30°C. Do not freeze'.

Safety and efficacy information

API used in this product is a well-known active substance with established efficacy and tolerability. A clinical overview has been provided, which is based on scientific literature. The overview justifies why there is no need to generate additional clinical data. Therefore, the member states agreed that no further clinical studies are required.

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. Dermazole 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>.

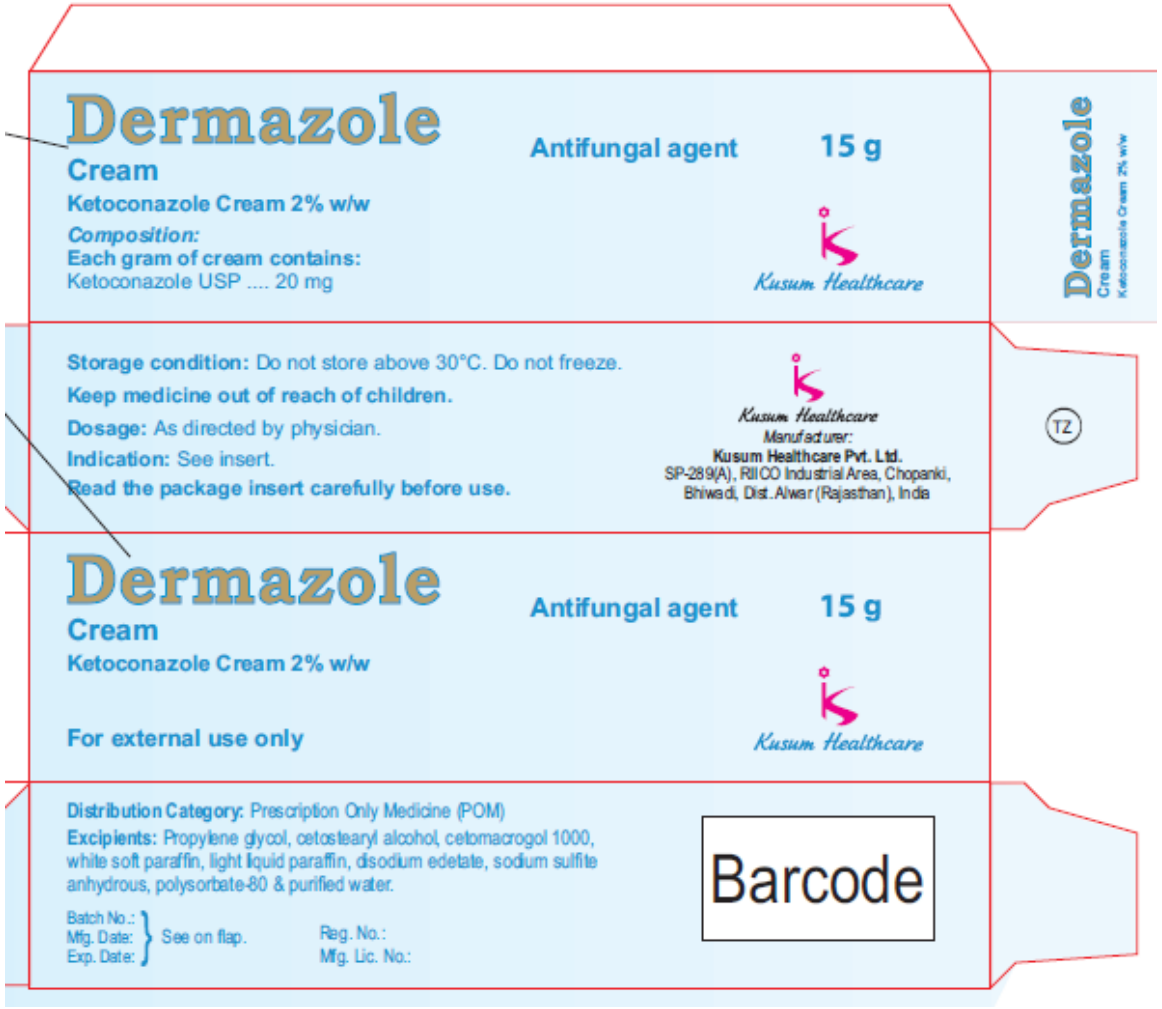
PART 5: CHANGE HISTORY

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