THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR BECLOGEN (CLOTRIMAZOLE 1%W/W, BECLOMETASONE 0.025%W/W AND GENTAMYCIN 0.1%W/W) CREAM

Version number 1.0
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1. Introduction

Beclogen cream is a generic medicine of Clotrimazole, Beclometasone and Gentamycin cream. Beclogen cream is a corticosteroid and anti-infective medicine belonging to Topical corticosteroid and anti-infective in combination group. Beclogen exerts its activity through the action of antifungal, corticosteroid and antibiotic. Clotrimazole is a broad-spectrum antifungal that inhibits fungi growth by damaging the cell membrane to lose its essential components. Gentamicin is an aminoglycoside antibiotic that kills bacteria by disrupting its ability to produce essential proteins for its growth. Beclometasone is a corticosteroid that produces an anti-inflammatory activity by blocking the production of prostaglandins. Beclogen is approved in Tanzania for use in <adults, children, elderly etc>.

1.1 Product details

Registration number	TAN 20 HM 0205
Brand name	Beclogen cream
Generic name, strength and form	Clotrimazole 1%w/w, Beclometasone 0.025%w/w and Gentamycin 0.1%w/w cream
ATC classification	D07AC01, D01AC01, D06AX07
Distribution category	POM
Country of origin	India
Associated product	N/A
Marketing Authorization Holder	Phillips Distributors Limited Plot No. 111, Nyerere Road, Vingunguti Industrial Area Tanzania
Local Technical Representative	Phillips Distributors Limited Plot No. 111, Nyerere Road, Vingunguti Industrial Area Tanzania

1.2 Assessment procedure

The application for registration of Beclogen was submitted n 2016. The product underwent full assessment. Assessment was completed in 5 rounds of evaluation. Beclogen was registered on 25/09/2020.

1.3 Information for users

Visual description of the finished product	White to off white soft cream
Primary packing material	Aluminium tube
Secondary packing materials	1 tube in a printed box with leaflet.
Shelf-life and storage condition	36 months Store in a dry place below 30^{o}C. Protect from

	light. Keep out of reach of children
Route of administration	Topical
Therapeutic indications	Beclogen Cream is indicated for the topical treatment of secondarily infected fungal infection of the skin and in infections associated with dermatoses viz. infectious eczematous dermatitis, acne, infected contact dermatitis

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 simplified information for patients.

Container labels
The product label information is presented in <English/Swahili>. Details in the secondary pack label include:
Brand name:
Composition: <generic name & strength, list of excipients (if applicable)>
Pack size: <primary & secondary pack>
Manufacturing details: <batch number, manufacturing date, expiry date>
Storage conditions: <state the condition as it appears on the label>
Manufacturer address: <physical address of release site>
Unique identifier: <state the unique identification used>
Special warnings/precautions or instructions for use: <include warnings or IFU if applicable>

The details of the primary pack include:
Brand name and strength:
Manufacturing details: <batch number, manufacturing date, expiry date>
Name of manufacturer: <name only>

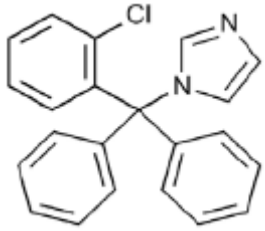
The content of the primary and secondary labels was aligned to the requirements of the Part V of the Compendium: Guidelines on Format and Content of Product Labels for Medicinal products. The label contains sufficient information for proper identification of the medicine and post marketing follow up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

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

General properties
Clotrimazole API is compendia in USP.
Molecular formula: $C_{22}H_{17}ClN_2$
Chemical name: 1H-Imidazole, 1-[(2-chlorophenyl) diphenyl methyl]
Structure:



Critical physico-chemical properties of the API were freely soluble in methanol, in acetone, in chloroform and in alcohol, practically insoluble in water.

Manufacture
The API manufacturing site, Amoli Organics Private Limited, Plot No. 322/4, 40 Shed Area, G.I.D.C., Vapi, District – Valsad,State - Gujarat, INDIA was noted to comply with WHO GMP requirements as evidenced by the GMP certificate issued by Food and Drug Administration of Gandhinagar, India. Clotrimazole 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/in-house standards and ICHQ3A. The parameters monitored during quality control are: description, solubility, identification, loss on drying, residue on ignition, heavy metals, limit of imidazole, limit of clotrimazole related compound A, assay, residual solvents and particle size. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system
The re-test period of Clotrimazole API is 60 months when packed in HMHDPE bag and strip sealed and stored at below 25°C.

Beclomethasone Dipropionate
Information on quality of the API was submitted in form of CEP.

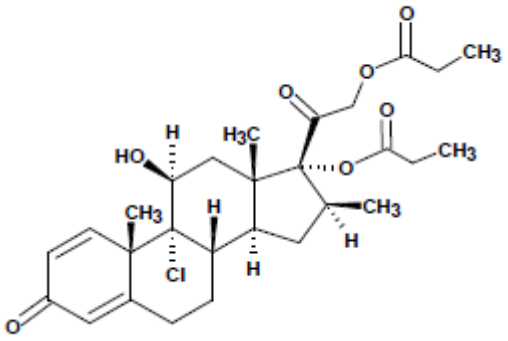
General properties

Beclomethasone Dipropionate API is compendia in BP.

Molecular formula: $C_{28}H_{37}ClO_7$

Chemical name: 9-chloro -11β-hydroxy-16β-methyl- 3, 20- dioxopregna-1, 4-diene-17, 21- diyl dipropanoate.

Structure:



Critical physico-chemical properties of the API were practically insoluble in water, freely Soluble in acetone, sparingly soluble in ethanol. (96%).

Manufacture

The API manufacturing site, Avik Pharmaceutical Ltd, 194, Arvind Chambers, Gauri Studio Compound, Western Express Highway, Andheri (E), Mumbai State: Maharashtra, Dist: -Thane, Maharashtra,India was noted to comply with WHO GMP requirements as evidenced by the GMP certificate issued by <state the issuing authority>. Beclomethasone Dipropionate API is manufactured by <chemical/fermentation> synthesis using <conventional/novel> 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 BP standards and ICHQ3A. The parameters monitored during quality control are appearance, solubility, identification, specific optical rotation, related substances, loss on drying and assay. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

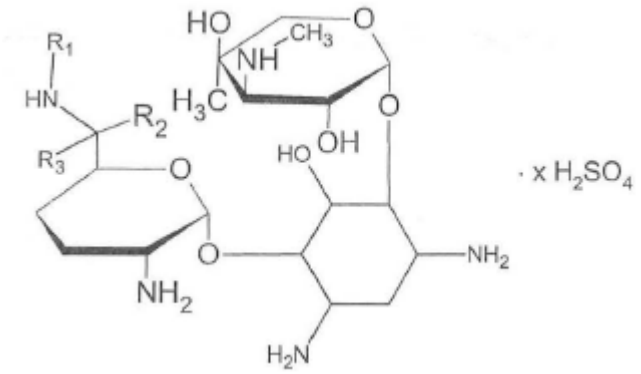
The <shelf-life/re-test> period of <molecule> API is <number> months when packed in polyethylene bag placed in a fibre or polyethylene drum and stored at <storage conditions>.

Gentamicin Sulphate

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

General properties

Gentamicin Sulphate API is compendia in USP/BP.
Molecular formula: $C_{21}H_{43}N_5O_7.H_2SO_4$
Chemical name:
0-3-deoxy-4-C-methyl-3-(methylamino)-(J-L-arabinopyranosyl-(1-6)-0-[2,6-diamino-2,3,4,6,-tetradeoxy-a-Derythro-hexopyr anosyl -(1-4)]-2-deoxy-D-streptamine.
Structure:



Critical physico-chemical properties of the API were freely soluble in water, practically insoluble in alcohol.

Manufacture
The API manufacturing site, Fujian Fukang Pharmaceutical Co., Ltd., Jiangyin Industrial Estate, 350309 , Fuqing, Fujian,The People's Republic of China was noted to comply with WHO GMP requirements as evidenced by the GMP certificate issued by <state the issuing authority>. Gentamicin Sulphate 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 BP standards and ICHQ3A. The parameters monitored during quality control are characters, identification, appearance of solution, pH, specific optical rotation (anhydrous substance), composition, related substances, methanol, sulfate (anhydrous substance), water, sulfated ash, bacterial endotoxins, assay and microbial enumeration. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system
The re-test period of Gentamicin Sulphate API is 48 months when packed in polyethylene bags (low-density) and stored at below 30°C.

Quality of the Finished Pharmaceutical Product

Formulation

Beclogen is a white to off white soft cream packed in 15g Aluminium tube. Beclogen contains Clotrimazole, Beclometasone dipripionate, Gentamycin sulfate and other ingredients listed hereafter chlorocresol, sodium dihydrogen phosphate dihydrate, propylene glycol, cetostearyl alcohol, macrogol cetostearyl ether, light liquid paraffin, white soft paraffin, methyl paraben, propyl paraben and purified water. 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.

Manufacture

The finished product was manufactured at Sava Healthcare Limited, Plot No :507- B to 512, G.I. D.C. Estate, Wadhwancity, Dist- Surendranagar, Gujarat, INDIA. The compliance of the site to TMDA GMP standards was confirmed through site inspection on <date of GMP compliance>.

Specifications

The FPP is non-compendia. The manufacturer controls the quality of the finished product as per in-house and ICHQ3B requirements. The parameters monitored during quality control are: description, identification, filled weight, pH, 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 ±2°C /75%±5% RH for 36 months and 40±2°C /75%±5% for 6 months. Based on the stability data presented, the approved shelf-life is 36 months when stored in 15 g collapsible aluminium Tube at below 30°C.

Safety and efficacy information

Safety and efficacy of Beclogen was established through reliance on the innovator product.

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. Beclogen 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