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MINISTRYOFHEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR ERYTHROKANT (ERYTHROMYCIN STEARATE BP 500MG) TABLETS

Version number 1.0
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1. Introduction

Erythrokant – 500 is a generic medicine of Erythromycin 500 mg tablets. Erythrokant – 500 is a macrolide antibiotic medicine belonging to J01FA01-Antibacterials for systemic use group. Erythrokant – 500 exerts is activity by binding to the 50S ribosomal sub-unit of susceptible microorganisms and suppresses protein synthesis. Erythrokant – 500 is approved in Tanzania for use in adults and children.

1.1 Product details

Registration number	TAN 20 HM 0208
Brand name	Erythrokant – 500
Generic name, strength and form	Erythromycin Stearate BP 500mg tablets
ATC classification	J01FA01
Distribution category	POM
Country of origin	India
Associated product	NA
Marketing Authorization Holder	S.K. AGE EXPORTS 3 A Shiv Sagar Estate, Dr Annie Besant Road, Worli, Mumbai 400018 Maharashtra, India Email: skhl@sk1932.com
Local Technical Representative	Abacus Pharma (A) Ltd. Plot No. 18C, Nyerere Road P.O.Box 12294, Dar Es Salaam, Tanzania

1.2 Assessment procedure

The application for registration of Erythrokant – 500 was submitted on 05/09/2014. The product underwent full assessment. Assessment was completed in 4 rounds of evaluation. Erythrokant – 500 was registered on 09/07/2020.

1.3 Information for users

Visual description of the finished product	White colour, film coated biconvex, oval shaped tablets, one side having break central line at middle, other side plain
Primary packing material	ALU/PVC blisters
Secondary packing materials	10 ALU/PVC blisters in a carton along with insert
Shelf-life and storage condition	24 months Store below 30°C

Route of administration	Oral
Therapeutic indications	For the prophylaxis and treatment of infections caused by erythromycin-sensitive organisms. Erythromycin is lightly effective in the treatment of a great variety of clinical infections such as: 1. Upper Respiratory Tract infections: tonsillitis, peritonsillar abscess, pharyngitis, laryngitis, sinusitis, secondary infections in influenza and common colds. 2. Lower Respiratory Tract infections: tracheitis, acute and chronic bronchitis, pneumonia (lobar pneumonia, bronchopneumonia, primary atypical pneumonia), bronchiectasis, Legionnaire's disease 4. Oral infections: gingivitis, Vincent's angina 5. Eye infections: blepharitis 6. Skin and soft tissue infections: boils and carbuncles, paronychia, abscesses, pustular acne, impetigo, cellulitis, erysipelas 7. Gastrointestinal infections: cholecystitis, staphylococcal enterocolitis 8. Prophylaxis: pre- and post- operative trauma, burns, rheumatic fever 9. Other infections: osteomyelitis, urethritis, gonorrhoea, syphilis, lymphogranuloma venereum, diphtheria, prostatitis, scarlet fever

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. 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

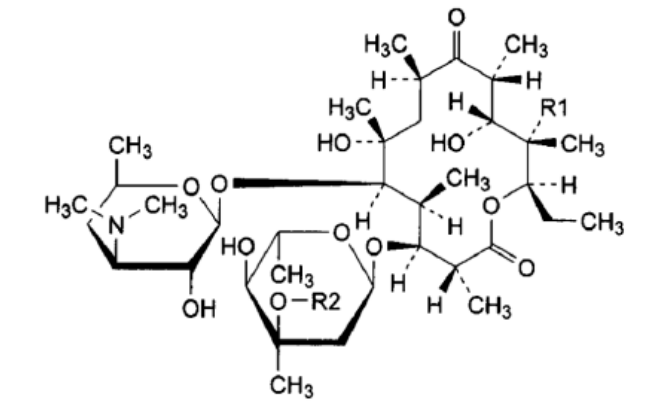
Quality of Active Pharmaceutical Ingredient(s)

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

General properties
Erythromycin Stearate API is compendia in USP/BP.

Molecular formula: $C_{37}H_{67}NO_{13}$,$C_{18}H_{36}O_2$
Chemical name:
(3R,4S,5S,6R,7R,9R,11R,12R,13S,14R)-6-[[3-(dimethylamino)-3,4,6-trideoxy -β-D-xylo-hexopyranosyl]oxy] 14 -ethyl-7,12,13- trihydroxy –3,5,7,9,11,13-hexamethyl –4-[(3-C-methyl –3-O –methyl –2,6dideoxy-α-L-ribo-hexopyranosyl)oxy]oxacyclotetradecane-2,1-dione.

Structure:



Erythromycin	Mol. Formula	R1	R2
A	$C_{55}H_{103}NO_{15}$	OH	CH_3
B	$C_{55}H_{103}NO_{14}$	H	CH_3
C	$C_{54}H_{101}NO_{15}$	OH	H

Critical physico-chemical properties of the API were practically insoluble in water, soluble in acetone, and in methanol. Solution may be opalescent.

Manufacture

The API manufacturing site, M/S Anuh Pharma Ltd, E-17/3-E17/4 M.I.D.C. Tarapur Boisar, Dist: Thane- 401506 Maharashtra,India was noted to comply with WHO GMP requirements as evidenced by the GMP certificate issued by <state the issuing authority>. Erythromycin 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: description, solubility, identification,free stearic acid, related substances,assay, water, sulphated ash, particle size, foreign matter, bulk density and tapped density.Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The re-test period of Erythromycin API is 36 months when packed in polyethylene bags and stored at 30°C.

Quality of the Finished Pharmaceutical Product

Formulation

Erythrokant – 500 is a White colour, film coated biconvex, oval shaped tablets, one side having break line at middle, other side plain. Erythrokant – 500 contains Erythromycin stearate and

other ingredients listed hereafter: maize starch (dry mix),microcrystalline cellulose , croscarmellose sodium, povidone K-30, docusate sodium, isopropyl alcohol, sodium starch glycolate, sodium lauryl sulphate, purified talc, colloidal anhydrous silica, titanium dioxide (wincoat white wt-1003) and dichloromethane. 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 S Kant Healthcare Ltd., 1802 – 1805, G. I. D. C, Phase III,Vapi – 396195, Valsad, Gujarat, India. The compliance of the site to TMDA GMP standards was confirmed through site inspection on 05-06/10/2018.

Specifications

The FPP is compendia in BP. The manufacturer controls the quality of the finished product as per BP and ICHQ3B requirements. The parameters monitored during quality control are: description, identification, dissolution,assay ,average weight, uniformity of weight, length, breadth, thickness, disintegration time, microbiological limit test, residual solvents and related substances. 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% and 30°C±2°C/75%±5% for 24 and 36 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 Alu/PVC blister at 30°C.

Safety and efficacy information

Safety and efficacy of Erythrokant – 500 was established through a bioequivalence trial. BE trial report number OS/ERST/11-18/02 was submitted.

In case of BE:

Study title	Bioequivalence Study Comparing Erythromycin Stearate Tablets BP 500 mg containing Erythromycin Stearate equivalent to Erythromycin 500 mg of S Kant Healthcare Limited, India with ERYTHROCIN 500 (Erythromycin Stearate) Tablets containing Erythromycin Stearate equivalent to Erythromycin 500 mg of Amdipharm UK Limited, UK
Study design	An open label, randomized, two-treatment, two-period, two-sequence, single dose, crossover, comparative bioequivalence study in healthy adult human male subjects under fasting conditions
Study site	Om Sai Clinical Research Pvt. Ltd. C.S.T. No.379/1-6, Karnal Chowki, Peth Bhag,

	Sangli - 416 416, Maharashtra, India	
Study dates	11-December-2018 and 29-December-2018 (clinical phase and analytical phase)	
Primary objective	To compare the rate and extent of absorption of Erythromycin Stearate after administration of Erythromycin Stearate Tablets BP 500 mg containing Erythromycin Stearate equivalent to Erythromycin 500 mg of S Kant Healthcare Limited, India with ERYTHROCIN 500 (Erythromycin Stearate) Tablets containing Erythromycin Stearate equivalent to Erythromycin 500 mg of Amdipharm UK Limited, UK under fasting condition in healthy adult human male subjects in a randomized crossover bioequivalence study	
Secondary objective	To monitor the safety and tolerability of a single dose of Erythromycin Stearate Tablets 500 mg when administered in 24 healthy human male subjects under fasting condition	
Number of participants	24	
Monitored parameters	Tmax, Cmax, AUCt, AUC inf	
Investigational medicinal products	Test Product Erythrokant – 500 of S Kant Healthcare Limited, India	Reference product Erythrocin® Tablets of Amdipharm UK Limited, UK
	Strength: 500 mg Batch number: EN8004 Expiry date: 12/2020	Strength: 500 mg Batch number: 6063165 Expiry date: 11/2020
Analytical method	LCMSMS	
Statistical method	SAS® software version 9.1-revision 9.1.3	

Efficacy results are summarized as follows:

Parameter	Test	Reference	% Ratio of geometric means	90 % Confidence interval	DF	CV (%)
AUC0-t (ng×hr/mL)	8.987	8.421	93.711	84.577 – 103.832%	0.289	20.913
AUC0-inf (ng×hr/mL)	9.264	8.671	93.598	84.739 – 103.383%	0.265	20.263
Cmax (ng/mL)	1.228	1.211	98.689	95.010 – 102.510%	0.557	7.675

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, Erythrokant – 500 is equivalent and interchangeable with Erythrocin® Tablets under acceptable in vivo experimental conditions.

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. Erythrokant – 500 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