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MINISTRYOFHEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR ERYTHROKANT-DS (ERYTHROMYCIN STEARATE 250MG/5ML) POWDER FOR ORAL SUSPENSION

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1. Introduction

Erythrokant-DS is a generic medicine of Erythromycin oral suspension. Erythrokant-DS is a macrolide antibiotic medicine belonging to J01FA01-Antibacterials for systemic use group. Erythrokant-DS exerts is activity by binding to the 50S ribosomal sub-unit of susceptible microorganisms and suppresses protein synthesis. Erythrokant is approved in Tanzania for use in <adults, children, elderly etc>.

1.1 Product details

Registration number	TAN 20 HM 0389
Brand name	Erythrokant-DS
Generic name, strength and form	Erythromycin Stearate 250mg/5ml powder for oral suspension
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-DS was submitted on 30/05/2014. The product underwent full assessment. Assessment was completed in 4 rounds of evaluation. Erythrokant was registered on 25/09/2020.

1.3 Information for users

Visual description of the finished product	White granules powder which on reconstitution with water up to 60 ml gives an orange suspension
Primary packing material	Amber coloured PET bottle
Secondary packing materials	
Shelf-life and storage condition	24 months

	Do not store above 30°C
Route of administration	Oral
Therapeutic indications	Erythromycin is indicated for the treatment / prophylaxis of infections caused by erythromycin-sensitive organisms:- • upper and lower respiratory tract infections • skin and soft tissue infections • bone infections • gastro–intestinal infections • oral/dental infections • eye infections • sexually transmitted diseases • prophylaxis of whooping cough and diphtheria • as an alternative to penicillin for staphylococcal infections in sensitive patients Consideration should be given to official guidance on the appropriate use of antimicrobial agents

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

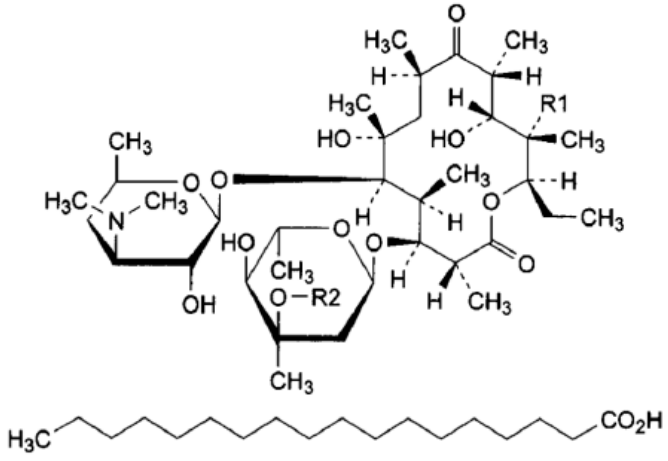
Quality of Active Pharmaceutical Ingredient(s)

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

General properties
Erythromycin Stearate API is compendial 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-DS is a white granules powder which on reconstitution with water up to 60 ml gives an orange suspension. Erythrokant-DS contains Erythromycin stearate and other ingredients listed hereafter: sucrose(pharma grade sugar), sodium carboxymethyl cellulose, methylparaben, disodium hydrogen phosphate, colloidal anhydrous silica, flavour strawberry powder, flavour raspberry powder, sodium citrate anhydrous, aspartame, colour sunset yellow FCF supra, xanthan gum.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. Ingredient, methylparaben and aspartame are of safety concern therefore appropriate warnings were included in the product label.

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 non-compendial. 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, pH, water, assay, fill weight 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 2 batches of the finished product stored at 30°C±2°C/75%±5% for 18 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 amber coloured PET bottle at 30°C.

Safety and efficacy information

Safety and efficacy of Erythrokant-DS was established through a bioequivalence trial. BE trial report number OS/ERST/10-19/25 was submitted.

In case of BE:

Study title	A randomized, single dose,open label, bioequivalence Study Comparing Erythromycin Stearate for oral suspension 250 mg/5ml containing Erythromycin Stearate equivalent to Erythromycin 250mg/5ml of S Kant Healthcare Limited, India with ERYTHROCIN 250 (Erythromycin Stearate) Tablets containing Erythromycin Stearate equivalent to Erythromycin 500 mg of Amdipharm UK Limited, UK in normal healthy human subjects under fasting conditions.
Study design	Randomized, balanced, open label, two-treatment, two-period, two-sequence, two-way crossover, single dose bioequivalence study in the healthy adult human male subjects under fasting condition, with at least 5 days washout period
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	
Primary objective	To compare the rate and extent of absorption of Erythromycin Stearate for Oral Suspension 250 mg/5mL containing Erythromycin Stearate equivalent to Erythromycin 250 mg/5mL of S Kant Healthcare Limited, India with ERYTHROCIN 250 (Erythromycin Stearate) Tablets containing Erythromycin Stearate equivalent to Erythromycin 250 mg of Amdipharm UK Limited, UK under fasting condition in healthy adult human male subjects in a randomised crossover bioequivalence study.
Secondary objective	To monitor the safety and tolerability of a single dose of Erythromycin Stearate for Oral Suspension 250 mg/5mL when administered in 24 healthy human male subjects under fasting

	condition	
Number of participants	24	
Monitored parameters	Tmax, Cmax, AUCt, AUCinf	
Investigational medicinal products	Test Product Erythrokant of S Kant Healthcare Limited, India	Reference product Erythrocin® Tablets of Amdipharm UK Limited, UK
	Strength: 125mg/5ml Batch number: EU8001 Expiry date: 08/2018	Strength: 250 mg Batch number: 6056574 Expiry date: 09/2020
Analytical method	LC-MSMS	
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)	10.986	11.105	101.077	91.321 – 111.877	0.858	20.695
AUC0-inf (ng×hr/mL)	11.428	11.810	103.344	93.830 – 113.822	0.565	19.669
Cmax (ng/mL)	1.464	1.480	101.079	98.678 – 103.538	0.451	4.851

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-DS 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-DS 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