THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR DEEXA-N (NEOMYCIN SULPHATE AND DEXAMETHASONE SODIUM PHOSPHATE) OPTHALMIC SOLUTION

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1. Introduction

DEEXA-N (Neomycin Sulphate and Dexamethasone Sodium Phosphate) ophthalmic solution has a dual effect: suppression of inflammation symptoms by the corticosteroidal component dexamethasone, and an anti-infective effect due to the presence of antibiotic, neomycin. Dexamethasone is a synthetic glucorticoid with potent anti-inflammatory activity. Neomycin is an aminoglycoside antibiotic that primarily exerts its effect on bacterial cells by inhibiting polypeptide assembly and synthesis on the ribosome. DEEXA-N (Neomycin Sulphate and Dexamethasone Sodium Phosphate) ophthalmic solution is approved in Tanzania for use in children and adults (including the elderly).

Product details

Registration number	TAN 23 HM 0266
Brand name	DEEXA-N
Generic name, strength, and form	Neomycin Sulfate 0.5% w/v & Dexamethasone Sodium Phosphate 0.1% w/v
ATC classification	S01CA01 Dexamethasone and Ant infectives
Distribution category	POM
Country of origin	India
Associated product	N/A
Marketing Authorization Holder	Lincoln Pharmaceuticals Limited Trimul Estate, Khatraj, Taluka: Kalol, District: Gandhinagar, Gujarat India
Local Technical Representative	Heko Pharmacy Ltd P.O. Box 2657, Dar Es Salaam

1.1 Assessment procedure

The application for registration of DEEXA-N was submitted in 27/01/2022. The product underwent abridged 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	A clear colourless to pale yellow colour clear solution
Primary packing material	HDPE, PP, PET, LDPE
Secondary packing materials	Printed carton box
Shelf-life and storage condition	24 months, Do not store above 30°C, Protect from light. Do not freeze.
Route of administration	Ophthalmic

Therapeutic indications	Neomycin Sulphate & Dexamethasone sodium phosphate ophthalmic solution is indicated for the short-term treatment of steroid responsive conditions of the eye when prophylactic antibiotic treatment is also required, after excluding the presence of fungal and viral disease. Microbiology: Anti-infective component (neomycin) is active against the common bacterial eye pathogens: Staphylococcus aureus, escherichia coli, haemophilus influenzae, Klebsiella/Enterobacter species and neisseria species. The product does not provide adequate coverage against: Pseudomonas aeruginosa, Serratia marcescens Streptococci, including Streptococcus pneumoniae

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: DEEXA-N

Composition: Neomycin Sulfate 0.5% w/v & Dexamethasone Sodium Phosphate 0.1% w/v

Pack size: 1 bottle

Manufacturing details: batch number, manufacturing date, and expiry date

Storage conditions: Do not store above 30°C, Protect from light. Do not freeze.

Manufacturer address: physical address of release site

Unique identifier: Not applicable

Special warnings/precautions or instructions for use:

The details of the primary pack include:

Brand name and strength: DEEXA-N (Neomycin Sulfate 0.5% w/v & Dexamethasone Sodium Phosphate 0.1% w/v)

Manufacturing details: batch number, manufacturing date and expiry date

Name of manufacturer: Lincoln Pharmaceuticals Limited

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 Ingredients

Information on the quality of the APIs was submitted in form of DMFs.

<u>Dexamethasone sodium phosphate</u>

General Information

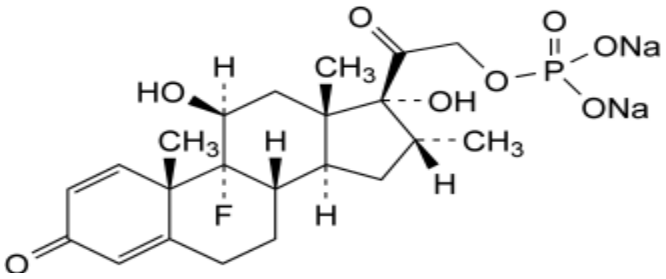
Dexamethasone sodium phosphate API is compendia in USP, BP, and Ph.Eur.

Molecular formula: $C_{22}H_{28}FNa_2O_8P$

Chemical name:

9-Fluoro-11β,17-dihydroxy-16α-methyl- 3,20-dioxopregna-1,4-dien-21-yl disodium phosphate

Structure:



General properties

The active substance is a white or almost white, very hygroscopic powder. No discussion for polymorphism and PSD is provided. Nonetheless, this is not considered important as the active substance is present in solution in the finished product. The active is present in the drug product dissolved in water, hence the polymorphic form and particle size distribution are not considered as critical quality aspects.

Manufacture

Dexamethasone sodium phosphate API manufacturer is Prachem Laboratories, Plot No. 3109, Phase-III, G.I.D.C. Chhatral, Ta. Kalol, Dist. Gandhinagar, Gujarat-382729, India. The manufacturing complies with GMP requirement as evidenced by the GMP certificates issued by the Food and Drugs Control Administration Gujarat State India. Dexamethasone sodium phosphate 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

Specifications

The API specifications were set as per BP standards and ICHQ3A. The parameters monitored during quality control are: appearance, solubility, identification by HPLC and IR, appearance of solution, pH, specific optical rotation, related substances, Inorganic phosphate, ethanol, water, assay, foreign matters. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The retest period of Dexamethasone sodium phosphate API is 36 months when packed in original container with storage condition ‘Store in cool & dry place’.

Neomycin Sulfate

General Information

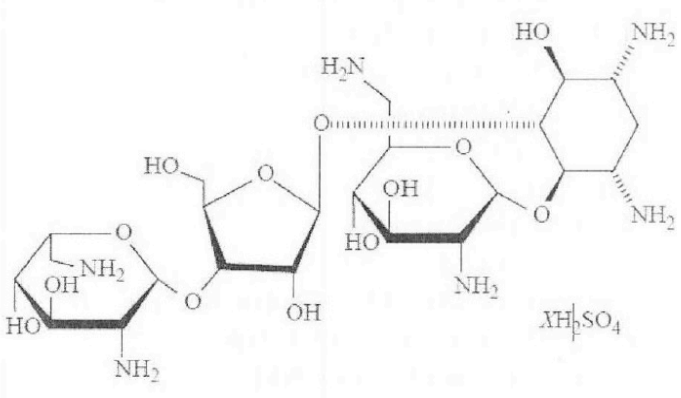
Neomycin Sulfate API is compendia in USP, BP, and Ph.Eur.

Molecular formula: $C_{23}H_{46}N_6O_{13}$, xH_2SO_4

Chemical name:

Mixture of sulfates of 2-deoxy-4-O-(2,6-diamino-2,6-dideoxy-α-D-glucopyranosyl)- 5 -O-[3 - O-(2,6-diamino-2,6-dideoxy-β-L idopyranosyl)-β- D-ribofuranosyl]-D-streptamine

Structure:



General properties

The active substance is a white or yellowish-white powder which very soluble in water, slightly soluble in alcohol, practically insoluble in acetone. No discussion for polymorphism and PSD is provided. Nonetheless, this is not considered important as the active substance is present in solution in the finished product. The active is present in the drug product dissolved in water, hence the polymorphic form and particle size distribution are not considered as critical quality aspects.

Manufacture

Neomycin Sulfate API manufacturer is Yichang Sanxia Pharmaceutical Co., Ltd, No.8, Ziyang Road, Dianjun District, Yichang, Hubei, China, Post code: 443002.The manufacturing complies with GMP requirements as evidenced by the GMP certificate issued by the Hebei Food and Drug Administration. Neomycin Sulfate 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

Specifications

The API specifications were set as per USP standards and ICHQ3A. The parameters monitored during quality control are: appearance, solubility, identification by HPLC and chemically reaction, sulfates, pH, loss on drying, assay, foreign matters. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The retest period of Neomycin Sulfate API is 48 months when packed in two layers of polyethylene bags and then one layer of partially transparent polyethylene bag in cardboard drum with storage condition ‘Keep container tightly closed’.

Quality of the Finished Pharmaceutical Product

Formulation

DEEXA-N ophthalmic solution is a white to off-white colored, oval shaped, beveled edges, biconvex, film coated tablets, plain on both sides.

DEEXA-N ophthalmic solution contains the Neomycin Sulphate and Dexamethasone Sodium Phosphate and other ingredients listed here after: disodium edetate, sodium bisulphite, creatinine, sodium citrate, sodium borate, polysorbate-80 (tween-80), benzalkonium chloride solution, hydrochloric acid, water for injections. 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 manufacturer is Lincoln Parenteral Limited, 11, Trimul Estate, Khatraj, Tal. Kalol, Dist. Gandhinagar, Gujarat, India. 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 in-house standards and ICH requirements. The parameters monitored during quality control are: description, identifications of the APIs, deliverable volume, pH, particulate matter, sterility, degradation products, assay, and osmolality. 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: 35 ± 5% RH for 24 months and 40± 2°C & RH: 25% ± 5% RH for 6 months. Based on the stability data presented, the approved shelf-life is 24 months when stored in original container with storage condition ‘Do not store above 30°C, Protect from Light. Do not freeze’.

Safety and efficacy information

DEEXA-N ophthalmic solution is a parenteral formulation and therefore fulfils the exemption mentioned in the part III: guidelines on therapeutic equivalence requirements, which states that a bioequivalence study is not required if the ophthalmic products prepared as aqueous solutions and containing the same active pharmaceutical ingredient(s) in the same concentration as currently registered products and which are administered by the same route(s). The quantitative composition of DEEXA-N ophthalmic solution entirely the same as the reference products in the market. Therefore, it may be considered as therapeutic equivalent, with the same efficacy/safety profile as known for the active substance of the reference medicinal product. The current product can be used instead of its reference product

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. DEEXA-N ophthalmic solution 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: