THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR VITAMIN A (VITAMIN A PALMITATE 100000 IU) SOFT GELATIN CAPSULES

Version number 1.0
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1. Introduction

Vitamin A capsules is a green colour, transparent oval shaped soft gelatin capsules containing slightly yellowish oily liquid containing the 100000 IU Vitamin A 9as Palmitate) per each capsule. Vitamin A, is a fat-soluble vitamin important in growth, development and maintenance of epithelial tissue and for vision. Vitamin A capsules is approved in Tanzania for use in all ages.

Product details

Registration number	TAN 23 HM 0298
Brand name	N/A
Generic name, strength, and form	Each soft gelatin capsule contains: Vitamin A 100000 IU (As Vitamin A Palmitate)
ATC classification	A11CC05
Distribution category	POM
Country of origin	India
Associated product	N/A
Marketing Authorization Holder	Indchemie Health Specialities Pvt. Ltd 510, Dr. E.Moses Road, Shah & Nahar Industries Estate, Worli, Mumbai 400018 India
Local Technical Representative	Jilichem (T) Limited P.O. Box .22400 Dar es Salaam Tanzania

1.1 Assessment procedure

The application for registration of Vitamin A capsules was submitted on 09/07/2022. The product underwent full assessment. Assessment was completed in 3 (three) rounds of evaluation and the product was registered on 01/06/2023.

1.2 Information for users

Visual description of the finished product	Green colour, transparent oval shaped soft gelatin capsules containing slightly yellowish oily liquid
Primary packing material	HDPE Bottle
Secondary packing materials	N/A
Shelf-life and storage condition	24 months, Do not store above 30 °C. Protect from light
Route of administration	Oral
Therapeutic indications	Vitamin A, a fat-soluble vitamin, is essential for growth, for the development and maintenance of epithelial tissue, and for vision, particularly in dim light. Vitamin A

	deficiency when the dietary intake is inadequate and is seen more frequently in young children than in adults. It is rare in developed countries but remains a major problem in developing countries. Prolonged deficiency leads to xeropthalmia or “dry eye”, the initial symptom of which may progress to severe eye lesions and blindness. Other symptoms include changes in the skin and mucous membranes. Vitamin A has also been used alone to treat various skin disorders including acne and psoriasis. It has been tried in patients with retinitis pigmentosa to retard the decline in retinal function. In Anaemia: there has been a study among pregnant women with nutritional anaemia that demonstrated a beneficial effect of Vitamin A on haemoglobin when given with iron supplementation. Diarrhoea: several of the large mortality trials already mentioned reported that Vitamin A supplementation was associated with reduced mortality attributed to diarrhoea, but did not. Measles: Vitamin A supplementation has an important role in the prevention of complications from measles. Two studies specially addressing vitamin A status and measles had found that complications such as pneumonia and diarrhoea were less common in children who had received supplement at the time of diagnosis than in those given a placebo. Meta-analysis of randomised trials concluded that a dose 200 000 units of vitamin A given on two consecutive says duced mortality in children with measles. WHO has recommended treating children in populations where vitamin A deficiency is common with high-dose vitamin A supplement during episodes of measles. A dose of 200000 units should given on two consecutive days to all children over 12 months of age. This should be followed by a further dose at least weeks later. Infants less

	than 6 months of age should receive doses of 50 000 units and those between 6 and 12 months should be given 100 000 units. Studies in the USA have indicated that even among well-nourished children from a developed country. Vitamin A deficiency in measles patients is in uncommon, and Vitamin A supplementation needs to consider in children risk. Shigellosis: A single high __ dose vitamin A supplement reduces the severity of acute shigellosis in children. Xeropthalmia: Vitamin A deficiency is responsible is man developing countries for visual problems which may culminat in xerophthalmia and blindness. Supplementation with vitamin A as recommended by status of the individual and act prophylactically against the development of xerophthalmia. For the treatment xerophthalmia (which includes night blindness, conjunctival xerosis with Bitot 's spots, corneal xerosis, corneal ulceration, and keratomalacia) WHO have stated that oral doses of vitamin A , are the treatment t of choir and should be given immediately the disorder is recognized. WHO have stated that oral doses of vitamin A , are the treatment t of choir and should be given immediately the disorder is recognised.

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:

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: Indchemie Health Specialities 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

General Information

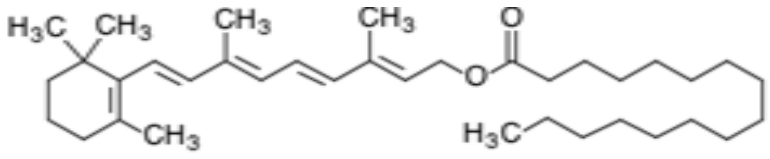
Vitamin A API is compendia in Ph.Eur., BP, USP.

Molecular formula: $CH_4N_2O_2$

Chemical name:

[(2E,4E,6E,8E)-3,7-Dimethyl-9-(2,6,6-trimethyl-1-cyclohexenyl) Nona 2,4,6,8-tetraenyl] hex decanoate

Structure:



General properties

Vitamin A is a light yellow to red oil, May be practically odorless or may have a mild fishy odour, but has no rancid odour or taste It dissolves in absolute alcohol and in vegetable oils; insoluble in water and in Glycerin.

Manufacture

Vitamin A API manufacturer is DSM Nutritional Products, Plot No. E-57, & E-58, Additional MIDC Anand Nagar, Ambernath – 421501, Maharashtra, India. The manufacturing complies with GMP requirements as evidenced by the GMP certificate issued by the Food & Drug

Administration Maharashtra. Vitamin A 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, identification (Chemical reaction and TLC), assay, absorbance ratio, residual solvents. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The re-test period of Vitamin A API is 36 months when packed in HDPE can with storage condition 'Do not store above 25°C'.

Quality of the Finished Pharmaceutical Product

Formulation

Vitamin A capsules is a green colour, transparent oval shaped soft gelatin capsules containing slightly yellowish oily liquid

Vitamin A capsules contains the Vitamin A other ingredients listed here after: gelatin, glycerin, sorbitol solution (70 %) non crystallizing, methylparaben, propylparaben brilliant blue fcf supra, diethyl ether, light liquid paraffin, refined soybean oil, purified water, butylated hydroxy anisole, butylated hydroxy toluene. 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 Indchemie Health Specialities Pvt. Ltd, Mahatma Gandhi Udyog Nagar, Dabhel, Daman (Union Territory) -396210 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 USP standards and ICH requirements. The parameters monitored during quality control are: Description, identification by TLC and chemical reaction, average net weight, uniformity of weight, disintegration time, loss on drying, uniformity of dosage unit, microbial enumeration, assays of API and preservatives. 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 24 months and 40± 2°C & RH: 75% ± 5% RH for 6 months. Based on the stability data presented, the approved shelf-life is 24 months when stored in HDPE container with storage condition 'Do not store above 30°C, protect from light'.

Safety and efficacy information

Therapeutic indications
Vitamin A is a fat-soluble vitamin essential for growth, development and maintenance of epithelial tissues and for vision as well as body's natural defence against illness and infection (the immune system) work properly. It's generally used for treatment and for prophylaxis of Vitamin A deficiency (Xeropthalmia).

Information provided in this section is acceptable and sufficient and is comparable to the information provided from literatures.

Refer: Martindale the Complete Drug Reference Thirty-sixth edition (Page; 1971 to 1973)

Posology and method of administration
The declared dose, dosage and route of administration and maximum standard dose both in adult and children in different therapeutic indications, patient's categories such as elderly is acceptable and was comparable to the information provided from literature search,

Refer: Martindale the Complete Drug Reference Thirty-sixth edition (Page; 1971 to 1973) and the comparator SmPC

Contraindications
Vitamin A is contraindicated to patients hypersensitive to vitamin A or any other component of a vitamin A containing pharmaceutical preparation. Local inflammatory reactions and severe anaphylactoid reactions can occur to those hypersensitive to vitamin A preparation. Information provided in this section is acceptable and considered sufficient

Special warnings and precautions for use
Information on this section were acceptable and were found to be in line with the information from literatures

Interaction with other medicinal products and other forms of interaction
Generally, Absorption of vitamin A from the gastrointestinal tract may be reduced by the presence of other medicinal drugs as per literature search including neomycin, colestyramine, or liquid paraffin. There is also an increased risk of hypervitaminosis A if vitamin A is given with synthetic retinoids such as acitretin, isotretinoin, and tretinoin.
Refer: Martindale the Complete Drug Reference Thirty-sixth edition (Page; 1971 to 1973)

Pregnancy and lactation
The use of vitamin is acceptable to pregnant women with maximum weekly allowable dose not exceeding 25000IU. Due to potential of teratogenic effects high dose of vitamin A should be avoided in possible pregnancy. Information provided is acceptable and comply with the information provided from Martindale The Complete Drug Reference Thirty-sixth edition (Page;

1971 to 1973).

Undesirable effects
Information about undesirable side effect following excessive administration of Vitamin A is sufficient presented and is comparable to the information provided from Martindale the Complete Drug Reference Thirty-sixth edition (Page; 1971 to 1973). Thus acceptable

Pharmacological properties
Pharmacodynamics and pharmacokinetics properties has been provided, Vitamin A substances are readily absorbed from the gastrointestinal tract but absorption may be reduced in the presence of fat malabsorption, low protein intake, or impaired liver or pancreatic function. Vitamin A esters are hydrolysed by pancreatic enzymes to retinol, which is then absorbed and re-esterified. Some retinol is stored in the liver. It is released from the liver bound to a specific α1-globulin (retinol-binding protein) in the blood. The retinol not stored in the liver undergoes glucuronide conjugation and subsequent oxidation to retinal and retinoic acid; these and other metabolites are excreted in urine and faeces.

Information provided in this section is acceptable and considered sufficient and was comparable to the information provided from literature searches;
Martindale The Complete Drug Reference Thirty-sixth edition (Page; 1971 to 1973).

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. Vitamin A capsules 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;