TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR PACLITAXEL 300 MG/50 ML CONCENTRATE FOR SOLUTION FOR INJECTION

Version number 1.0

14th April, 2022

P. O. Box 77150, EPI Mabibo, Off Mandela Road, Dar es Salaam, Tanzania
Tel: +255-22-2450512/2450751/ 2452108; Fax: +255-22-2450793
Email: info@tmda.go.tz; Website: mwww.tmda.go.tz

1. Introduction

Paclitaxel is an Anticancer medicine belonging to antineoplastic agents, Antineoplastic agent/taxanes group. Paclitaxel is an antimicrotubule agent that promotes the assembly of microtubules from tubulin dimers and stabilises microtubules by preventing depolymerisation. This stability inhibits the normal dynamic reorganisation of the microtubule network, which is essential for vital interphase and mitotic cellular functions. In addition, paclitaxel induces abnormal arrays or bundles of microtubules throughout the cell cycle and multiple asters of microtubules during mitosis.

Paclitaxel is approved in Tanzania for use in adults only.

1.1 Product details

Registration number	TAN 22 HM 0092
Brand name	Paclitaxel
Generic name, strength and form	Paclitaxel 300 mg/50 mL concentrate for solution for Injection
ATC classification	ATC Code: L01CD01 Antineoplastic agent/taxanes
Distribution category	POM
Country of origin	Australia
Associated product	State any other product of formulation, strength or site that is linked or associated with the product if applicable
Marketing Authorization Holder	Pfizer Laboratories Limited, Kenya 1st Floor Vienna Court, State House Crescent Road, Nairobi Kenya Telephone: 0706994801 Email: louiseakeyo.ongare@pfizer.com
Local Technical Representative	Macnaughton Limited Mek one Plaza, Plot no 4/1 & 8/1, P.O. Box 79400, Dar es Salaam, Tanzania

1.2 Assessment procedure

The application for registration of Paclitaxel was submitted on 1st July 2020. The product underwent abridged, joint EAC assessment. Assessment was completed in 2 rounds of evaluation. Paclitaxel was registered on 11th April, 2022

1.3 Information for users

Visual description of the finished product	Clear colorless to pale yellow solution free from visible particulates, presented in a 20 mL clear Type I glass vial, closed with elastomeric closures and aluminum seals with flip-off tops.

Primary packing material	Type I glass vial, with elastomeric closures and aluminum seals
Secondary packing materials	Cardboard carton box
Shelf-life and storage condition	24 months, "Do not store above 30ºC"
Route of administration	Intravenous
Therapeutic indications	Paclitaxel is indicated for the treatment of ovarian cancer, breast cancer, advanced Non-Small Cell Lung Cancer (NSCLC) and acquired immunodeficiency syndrome (AIDS) related Kaposi's Sarcoma (KS)

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 and French. Details in the secondary pack label include:
Brand name: Paclitaxel

Composition: Paclitaxel 300 mg/50 mL concentrate for solution for Injection

Pack size: 1 vial of 50 mL

Manufacturing details: batch number, manufacturing date, expiry date

Storage conditions: Do not store above 25ºC

Manufacturer address: Hospira Australia Pty Ltd, 1-5, 7-23 and 25-39 Lexia Place, MULGRAVE VIC 3170, Australia

Unique identifier: NA

Special warnings/precautions or instructions for use: NA

The details of the primary pack include:
Brand name and strength: Paclitaxel

Manufacturing details: batch number, manufacturing date, expiry date

Name of manufacturer: Hospira Australia Pty 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.
Describe any approved deviation to the requirements and the justification for the deviation.

Mock labels are appended as annex I

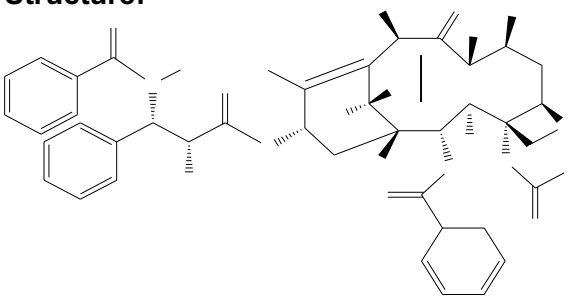
3. Scientific discussion

Quality of Active Pharmaceutical Ingredient(s)

Information on quality of the API was submitted in form of CEP

General Information
Paclitaxel API is compendia in USP/BP
Molecular formula: C47H51NO14
Chemical name: 5β,20-epoxy-1,7β-dihydroxy-9-oxotax-11-ene-2α,4,10β,13α-tetrayl 4,10-diacetate 2-benzoate 13-[(2R,3S)-3-(benzoylamino)-2-hydroxy-3-phenylpropanoate)]

Structure:



Physico-chemical properties of the API

Paclitaxel is a white to off-white crystalline powder that is practically insoluble in water, sparingly soluble in Ethanol and Isopropyl Alcohol, soluble in Methanol, Acetone and Ethyl Acetate.

The active substance shows polymorphism. Single polymorphic form of Paclitaxel has been identified: A hydrated form (β-form). The drug substance exhibit stereoisomerism due to the presence of 11 defined atom stereocenter count.

Particle size data for Paclitaxel produced from fermentation was acquired using a Malvern instrument for d10 (µm), d50 (µm) and d90 (µm).

Manufacture

The API manufacturing site is Phyton Biotech GmbH Alter Postweg 1, 22926 Ahrensburg, Germany was noted to comply with GMP requirements as evidenced by the CEP certificate issued by EDQM. Paclitaxel API is manufactured by fermentation 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, in-house standards and ICHQ3A. The parameters monitored during quality control are: appearance of solution (Ph. Eur.), identification (IR, HPLC), specific optical rotation (Ph. Eur.), related substances (HPLC), heavy metals (Ph. Eur.), water content (Ph. Eur.), assay (Ph. Eur.), residue on ignition (Ph. Eur), residual solvents (GC), total aerobic microbial count (Ph. Eur.), microbial enumeration test (Ph. Eur) and bacterial endotoxins (Ph. Eur.). Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The re-test period of Paclitaxel API is 36 months when packed in amber glass bottle closed with a polyethylene under cap and plastic screw cap, placed in a double polyethylene bag and stored at recommended storage condition.

Quality of the Finished Pharmaceutical Product

Formulation

Paclitaxel is a clear colorless to pale yellow solution free from visible particulates, presented in a clear type I glass vial, closed with elastomeric closures and aluminum seals with flip-off tops. Paclitaxel contains Paclitaxel and other ingredients listed here after: Polyoxyl, castor oil, Citric acid (anhydrous) and Dehydrated alcohol. 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 < Hospira Australia Pty Ltd., 1 – 5, 7 – 23 and 25 - 39 Lexia Place, Mulgrave, Victoria, 3170, Australia. The compliance of the site to TMDA GMP standards was confirmed through desk-review.

Specifications

The FPP is compendia in USP. The manufacturer controls the quality of the finished product as per in-house and ICHQ3B requirements. The parameters monitored during quality control are: appearance of the solution (visual), Identification (HPLC, TLC), pH (USP), assay (HPLC), Related Substances (HPLC), Particulate Matter (USP), Sterility (USP), Bacterial Endotoxins (USP) and fill volume (USP). 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 25°C/60 % RH, 30°C/65 % RH and 30°C/75 % RH for 36 months and <40°C/75 % RH for 6 months. Based on the stability data presented, the approved shelf-life is 36 months when stored in 50 mL type I glass vial, closed with elastomeric closures and aluminum seals with flip-off tops at 30ºC.

Safety and efficacy information

No data was provided to support the clinical efficacy of the product, however based on the formulation type and route of administration the product meet the criteria of waiving the submission of clinical data. Therefore, the safety and efficacy of Paclitaxel was established through published literature.

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. Paclitaxel 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

NA

PART 5: CHANGE HISTORY

Version number	Date	Description of update	Section(s) Modified	Approval date

Annex I: Mock up label