TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR PLATIFIRST 50 MG/50 ML (CISPLATIN 50MG/50ML) INJECTION

Version number 1.0

14 April, 2022

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1. Introduction

Platifirst 50 mg/50 ml is a generic medicine of innovator product Platinol 1mg/ml konsentrat til infusjonsvæske (Bristol-Myers Squibb, Norway). Platifirst 50 mg/50 ml is a platinum-based anti-neoplastic agent. Platinum-based agents cause intrastrand and interstrand crosslinks between purine bases of DNA, resulting in contortion of the DNA molecule. It is widely accepted that this DNA damage induces apoptosis, but there may also be other mechanisms involved in the cytotoxic effects of cisplatin. Platifirst 50 mg/50 ml is approved in Tanzania for use in adults and children.

1.1 Product details

Registration number	TAN 21 HM 0259
Brand name	Platifirst 50 mg/50 ml
Generic name, strength and form	Each single vial of 50 ml concentrate for solution for infusion contains 50 mg of cisplatin
ATC classification	Other antineoplastic agents, Platinum compounds (L01XA01)
Distribution category	POM
Country of origin	India
Associated product	Platifirst 10 mg/10 ml
Marketing Authorization Holder	VHB Medi Sciences Ltd 50 AB, Govt industrial Estate, Charkop, Kandivali (W) Mumbai-400067, India
Local Technical Representative	Planet Pharmaceuticals Limited P.O. Box: 38328 Dar-es-Salam

1.2 Assessment procedure

The application for registration of Platifirst 50 mg/50 ml was submitted on 10 February, 2021. The product underwent full assessment. Assessment was completed in 2 (two) rounds of evaluation and the product was registered on 03 June, 2021.

1.3 Information for users

Visual description of the finished product	A clear colorless to pale yellow solution
Primary packing material	50 mL USP type I glass vial, amber coloured
Secondary packing materials	A printed carton box
Shelf-life and storage condition	24 months, Store below 30°C. Protected from light. Do not Refrigerate
Route of administration	intravenously by infusion administration only
Therapeutic indications	Cisplatin is intended for the treatment of: - advanced or metastasised testicular cancer - advanced or metastasised ovarian cancer - advanced or metastasised bladder carcinoma

	- advanced or metastasised squamous cell carcinoma of the head and neck - advanced or metastasised non-small cell lung carcinoma - advanced or metastasised small cell lung carcinoma Cisplatin is indicated in the treatment of cervical carcinoma in combination with other chemotherapeutics or with radiotherapy. Cisplatin can be used as monotherapy and in combination therapy

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: Platifirst 50 mg/50 ml

Composition: Each ml contains: Cisplatin 1.0mg, Sodium Chloride 9mg, and Water for Injection q.s

Pack size: 1 vial

Manufacturing details: batch number, manufacturing date and expiry date

Storage conditions: Store below 30°C. Protected from light. Do not Refrigerate

Manufacturer address: physical address of release site

Unique identifier: Not applicable

Special warnings/precautions or instructions for use:
Solution with precipitate to be discarded.
Discard unused portion.
Handle the Injection with great care since it is a potent cytotoxic agent.
Cisplatin Injection that may come in contact with needles or IV set containing aluminum parts should not be administered.
It is dangerous to take this preparation except under the Medical Supervision.
To be supplied against demand from Cancer hospitals, Institutions and prescription of a Cancer Specialist only

The details of the primary pack include:

Brand name and strength: Platifirst 50 mg/50 ml

Manufacturing details: batch number, manufacturing date and expiry date

Name of manufacturer: VHB Medi Sciences 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(s)

Information on quality of the API was submitted in form of DMF.

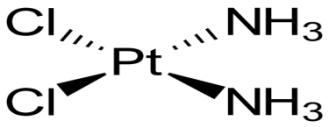
General Information

Cisplatin API is compendia in USP and BP

Molecular formula: $[PtCl_2(NH_3)_2]$

Chemical name:
cis-diamminedi-chloroplatinum (II)

Structure:



General properties

Cisplatin is a yellow powder or yellow or orange-yellow crystals, slightly soluble in water, sparingly soluble in dimethylformamide, practically insoluble in alcohol.

No polymorphic forms of Cisplatin are known. 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

Cisplatin API manufacturer is Sun Pharmaceutical Industries Ltd, A-7/A-8, M.I.D.C., Industrial Area, Ahmednagar-414111, Maharashtra, India. The manufacturing complies with GMP requirements as evidenced by the GMP certificate issued by Maharashtra Food and Drugs

Administration-India. Cisplatin 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 and in-house standards and ICHQ3A. The parameters monitored during quality control are: Appearance, Solubility, Identification, Appearance of solution, pH, Silver, Bacterial endotoxin, Related substances, Assay, and Residual solvents (GC). Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The re-test period of Cisplatin API is 72 months when packed in transparent polyethylene bags and stored in airtight container, protected from light.

Quality of the Finished Pharmaceutical Product

Formulation

Platifirst 50 mg/50 ml is a clear, colourless to pale yellow solution

Platifirst 50 mg/50 ml contains the API Cisplatin and other ingredients listed here after: mannitol, sodium chloride, hydrochloric acid and 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 VHB Medi Sciences Ltd, Plot No- 20-22 & 49-51, IIE, Sector-5, Sidcul, Pantnagar-263 145, Uttarakhand, India. The compliance of the site to TMDA GMP standards was confirmed through site inspection on 27th February, 2019.

Specifications

The FPP is subject to USP and BP. The manufacturer controls the quality of the finished product as per BP and in-house standards and ICH requirements. The parameters monitored during quality control are: Description, Identification, Extractable volume, pH, Related substances, Assay, Particulate matter (Visible and Sub-visible), Bacterial endotoxins, and Sterility. 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 packed in 50 mL USP type I glass vial, amber coloured with storage condition ‘Store below 30º C. Protected from light. Do not Refrigerate’.

Safety and efficacy information

No bioequivalence study was submitted to support the application.

The product concerned by the application contains the same active ingredient in the same concentration as the innovator product Platinol 1mg/ml konsentrat til infusjonsvæske (Bristol-Myers Squibb, Norway). It has an identical qualitative and quantitative composition in terms of the active substance as its the innovator product.

The product is aqueous concentrate for solution for infusion and contains Cisplatin as an active substance. Excipients are mannitol, sodium chloride, hydrochloric acid and water for injections. Due to the parenteral administration mode, bioequivalence can be concluded without further studies and as the composition is the same, no differences in non-clinical or clinical effects are possible.

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. Platifirst 50 mg/50 ml 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

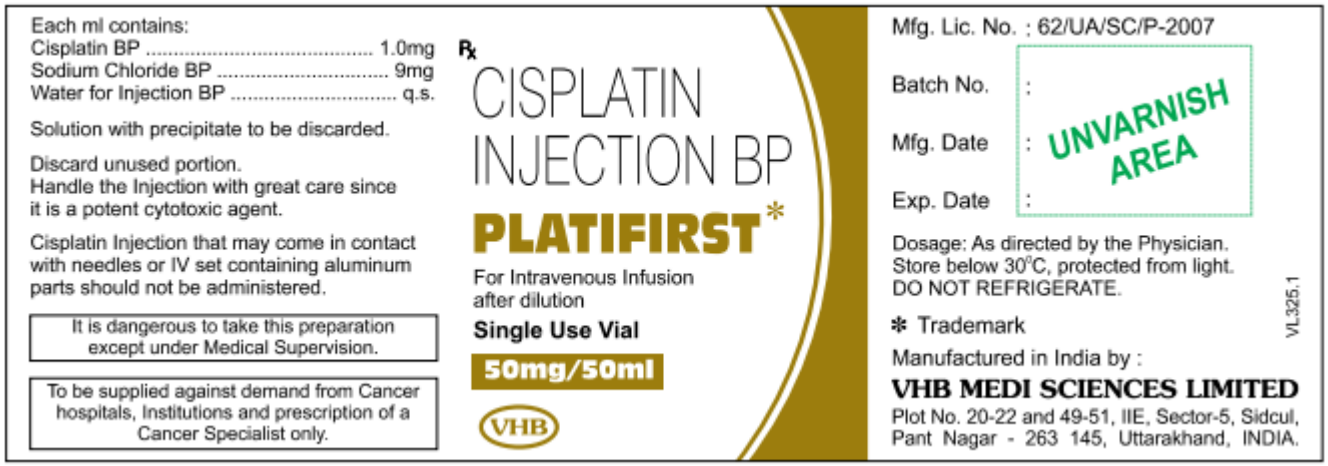
NA

PART 5: CHANGE HISTORY

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

Annex I: Mock up labels;

Primary pack label;



Secondary pack label;