SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

Docetaxel 20 mg/0.5 mL solution for injection
CP-Docetaxel 20

Docetaxel 80 mg/2 mL solution for injection
CP-Docetaxel 80

Docetaxel 120mg/ 3 mL solution for injection
CP-Docetaxel 120

2. Qualitative and quantitative composition

Each mL of solution contains 40 mg of docetaxel (as trihydrate).

For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Solution for injection.

A pale-yellow viscous liquid.

4. Clinical particulars

4.1 Therapeutic indications

Breast Cancer
Docetaxel is indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of prior chemotherapy and in combination with doxorubicin and cyclophosphamide is indicated for the adjuvant treatment of patients with operable node-positive breast cancer.

Non-Small Cell Lung Cancer
Docetaxel as a single agent is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of prior platinum-based chemotherapy. Docetaxel in combination with cisplatin is indicated for the treatment of patients with unresectable, locally advanced or metastatic non-small cell lung cancer who have not previously received chemotherapy for this condition.

Prostate Cancer
Docetaxel in combination with prednisone is indicated for the treatment of patients with androgen-independent (hormone-refractory) metastatic prostate cancer.

Gastric Adenocarcinoma
Docetaxel in combination with cisplatin and fluorouracil is indicated for the treatment of patients with advanced gastric adenocarcinoma, including adenocarcinoma of the gastroesophageal junction, who have not received prior chemotherapy for advanced disease.

Head and Neck Cancer
Docetaxel in combination with cisplatin and fluorouracil is indicated for the induction treatment of patients with locally advanced squamous cell carcinoma of the head and neck (SCCHN).

4.2 Posology and method of administration

Premedication Regimen
All patients should be premedicated with oral corticosteroids such as dexamethasone 16 mg per day (e.g., 8 mg BID) for 5 days starting 1 day prior to docetaxel administration in order to reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions.

Breast Cancer
For treatment of patients with locally advanced or metastatic carcinoma of the breast after progression during anthracycline-based therapy for metastatic disease or relapse during anthracycline-based adjuvant therapy, the recommended dose of docetaxel is 60-100 mg/m2 administered intravenously over one hour every three weeks.

Non-Small Cell Lung Cancer
For treatment of patients with advanced or metastatic non-small cell lung cancer after the failure of prior platinum-containing therapy, the recommended dose of docetaxel is 75-100 mg/m2 I.V. over one hour every 3 weeks.

Prostate cancer
For hormone-refractory metastatic prostate cancer, the recommended dose of docetaxel is 75 mg/m2 every 3 weeks as a 1-hour IV infusion. Prednisone 5 mg orally twice daily is administered continuously.

Gastric adenocarcinoma
For gastric adenocarcinoma, the recommended dose of docetaxel is 75 mg/m2 as a 1 hour IV infusion, followed by cisplatin 75 mg/m2, as a 1 to 3 hour IV infusion (both on day 1 only), followed by fluorouracil 750 mg/m2 per day given as a 24-hour continuous IV infusion for 5 days, starting at the end of the cisplatin infusion. Treatment is repeated every 3 weeks.

Head and Neck Cancer
Induction chemotherapy followed by radiotherapy - For the induction treatment of locally advanced inoperable SCCHN, the recommended dose of docetaxel is 75 mg/m2 as a 1 hour IV infusion followed by cisplatin 75 mg/m2 IV over 1 hour, on day one, followed by fluorouracil as a continuous IV infusion at 750 mg/m2 per day for five days. This regimen is administered every 3 weeks for 4 cycles.

Following chemotherapy, patients should receive radiotherapy.

Induction chemotherapy followed by chemoradiotherapy - For the induction treatment of patients with locally advanced (unresectable, low surgical cure, or organ preservation) SCCHN, the recommended dose of docetaxel is 75 mg/m2 as a 1 hour IV infusion on day 1, followed by cisplatin 100 mg/m2 administered as a 30-minute to 3 hour infusion, followed

by fluorouracil 1000 mg/m2/day as a continuous infusion from day 1 to day 4. This regimen is administered every 3 weeks for 3 cycles.

Following chemotherapy, patients should receive chemoradiotherapy.

Dosage Adjustments During Treatment
Patients who are dosed initially at 100 mg/m2 and who experience either febrile neutropenia, neutrophils < 500 cells/mm3, severe or cumulative cutaneous reactions, or severe peripheral neuropathy during docetaxel therapy should have the dosage adjusted from 100 mg/m2 to 75 mg/m2 if the patient continues to experience these reactions the dosage should either be decreased from 75 mg/m2 to 55 mg/m2 or the treatment should be discontinued.

Conversely, patients who are dosed initially at 60 mg/m2 and do not experience febrile neutropenia, neutrophils < 500 /mm3 for more than one week, severe or cumulative cutaneous reactions or severe peripheral neuropathy during docetaxel therapy may tolerate higher doses.

Preparation of the Infusion solution
Transfer the content of the solvent to the concentrate vial, shake and dilute with 0.9% sodium chloride or 5% dextrose to a final concentration of 0.3-0.9 mg/ml. Docetaxel infusion solution should be administered intravenously as a one-hour infusion under ambient room temperature and lighting conditions.

4.3 Contraindications
Docetaxel is contraindicated in patients who have a history of severe hypersensitivity reactions to docetaxel or other drugs formulated with polysorbate 80. Docetaxel should not be used in patients with neutrophil counts of < 1,500 cells/mm3.

4.4 Special warnings and precautions for use

General: Responding patients may not experience an improvement in performance status or therapy and may experience worsening. The relationship between changes in performance status, response to therapy and treatment-related side effects has not been established.

Hematologic Effects: In order to monitor the occurrence of myelotoxicity, it is recommended that frequent peripheral blood cell counts be performed on all patients receiving docetaxel. Patients should not be retreated with subsequent cycles of docetaxel, until neutrophils recover to a level of > 3 1,500 cells/mm and platelets recover to a level> 100,000 3 cells/mm.

A 25% reduction in the dose of docetaxel is recommended during subsequent cycles following severe neutropenia 3 (<500 cells/mm) lasting 7 days or more, febrile neutropenia, or grade 4 infections in a docetaxel cycle.

Hypersensitivity Reactions
Hypersensitivity reactions may occur within a few minutes following initiation of a docetaxel infusion. if minor reactions such as flushing or localized skin reactions occur, interruption of therapy is not required.

More severe reactions, however, require the immediate discontinuation of docetaxel and aggressive therapy. All patients should be premedicated with an oral corticosteroid prior to the initiation of the infusion of docetaxel.

Cutaneous
Localized erythema of the extremities with oedema followed by desquamation has been observed. In case of severe skin toxicity, an adjustment in dosage is recommended.

Fluid Retention
Severe fluid retention has been reported following docetaxel therapy. Patients should be premedicated with oral corticosteroids prior to each docetaxel administration to reduce the incidence and severity of fluid retention.

Patients with pre-existing effusions should be closely monitored from the first dose for the possible exacerbation of the effusions. The median cumulative dose to 2 onset of moderate or severe fluid retention was 705 mg/m in patients receiving premedication. Patients developing peripheral oedema may be treated with standard measures, e.g., salt restriction and oral diuretic(s).

Neurologic
Severe neurosensory symptoms (paresthesia, dysesthesia, pain) were observed among 7% of patients with anthracycline-resistant breast cancer. When these occur, dosage must be adjusted. If symptoms persist, treatment should be discontinued.

Asthenia
Severe asthenia has been reported in 11.1 % of the patients but has led to treatment discontinuation in only 2.6% of the patients. Severe asthenia was reported in 23% of patients with anthracycline-resistant breast cancer and 5.5% of the 786 cycles received.

Symptoms of fatigue and weakness may last a few days up to several weeks and may be associated with deterioration of performance status in patients with progressive disease.

WARNINGS
Docetaxel should be administered under the supervision of a qualified physician experienced in the use of antineoplastic agents. Appropriate management of complications is possible only when adequate diagnostic and treatment facilities are readily available.

4.5 Interaction with other medicinal products and other forms of interaction
There have been no formal clinical studies to evaluate the drug interactions of docetaxel with other medications. Docetaxel may be modified by the concomitant administration of compounds that induce, inhibit or are metabolized by cytochrome P450 3A4, such as cyclosporine, terfenadine, ketoconazole, erythromycin, and troleandomycin. Caution should be exercised with these drugs when treating patients receiving docetaxel as there is a potential for a significant interaction.

4.6 Fertility, pregnancy and lactation

Pregnancy: Pregnancy Category D.

Docetaxel can cause foetal harm when administered to pregnant women.

Nursing Mothers: It is not known whether docetaxel is excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from docetaxel, mothers should discontinue nursing prior to taking the drug.

Paediatric Use: The safety and effectiveness of docetaxel in pediatric patients have not been established.

4.7 Effects on the ability to drive and use machines
No studies of the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Hematologic
Bone marrow suppression is the major dose-limiting toxicity of docetaxel. Neutropenia is reversible and not cumulative. The median day to nadir was 8 days, while the median duration of severe neutropenia (<500 cells/mm) was 7 days. Among patients with normal liver function treated with docetaxel, severe neutropenia occurred in 76% and lasted for 7 days in 4.3% of cycles. Anaemia was reported in 89.5 % with severe cases being reported in 8.4% of the patients).

Hypersensitivity Reactions
Hypersensitivity reactions requiring discontinuation of the docetaxel infusion were reported in patients who did not receive premedication. Severe hypersensitivity reactions characterized by hypotension and/or bronchospasm, or generalized rash/erythemas have been observed in only 0.9% of patients with normal liver function receiving the recommended premedication regimen and none of these patients had to discontinue therapy.

Minor events, including flushing, a rash with or without pruritis, chest tightness, back pain, dyspnea, drug fever, or chills, have been reported and resolved after discontinuing the infusion and appropriate therapy.

Fluid Retention
Events such as oedema and weight gain and, less frequently, pleural effusion, pericardial effusion or ascites have been described.

Cutaneous
Reversible cutaneous reactions characterized by a rash including localized eruptions, mainly on the feet and/or hands, but also on the arms, face or thorax, usually associated with pruritus, have been observed.

Neurologic
Neurosensory symptoms characterized by paresthesia, dysesthesia or pain (including burning sensation) have been reported in patients receiving docetaxel.

Gastrointestinal
Gastrointestinal reactions (nausea, and/or vomiting, and/or diarrhoea were generally mild to moderate and severe reactions occurred in 8.2% of the patients. Stomatitis was reported in 42.3% of patients receiving docetaxel. Severe reactions were observed in 5.3% of patients.

Cardiovascular
Hypertension occurred in 3.6% of the patients; 3.4% required treatment. Clinically meaningful events such as heart failure, sinus tachycardia, atrial flutter, dysrhythmia, unstable angina, pulmonary oedema and hypertension occurred rarely.

Infusion Site Reactions
Infusion site reactions were generally mild and consisted of hyperpigmentation, inflammation, redness or dryness of the skin, phlebitis, extravasation, or swelling of the vein.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the e-PV desktop applications (https://drive.google.com/file/d/16hwTz0587ZWtSWadbBAMwQPOD_KSExZP/view) or search for e-PV Mobile applications on the Google Play or Apple App Store.

4.9 Overdose
There is no known antidote for docetaxel overdosage. In case of overdosage, the patient should be kept in to specialized unit where vital functions can be closely monitored. Anticipated complications of overdosage include bone marrow suppression, peripheral neurotoxicity, mucositis, severe neutropenia, mild asthenia, cutaneous reactions, and mild paresthesia. There are two reports of overdose, one patient received 150 mg/m2 and the other received 200 mg/m2 as one-hour infusions. Both patients experienced severe neutropenia, mild asthenia, cutaneous reactions, and mild paresthesia and recovered without incident.

5. Pharmacological properties

5.1 Pharmacodynamic properties
Pharmacological classification: 9.4 Miscellaneous cytotoxic agents.

Docetaxel is an anti-neoplastic agent that acts by disrupting the microtubular network in cells which is essential for mitotic and interphase cellular functions. Docetaxel binds to free tubulin and promotes the assembly of tubulin into stable microtubules while simultaneously inhibiting their disassembly. This leads to the production of microtubule bundles without normal function and to the stabilization of microtubules, which results in the inhibition of mitosis in cells. Docetaxel's binding to microtubules does not alter the number of protofilaments in the bound microtubules, a feature, which differs from most spindle poisons currently in clinical use.

5.2 Pharmacokinetic properties

Absorption
After administration of 20 mg/m2 to 115 mg/m2 the area under the curve (AUC) is dose-proportional following doses of 70 mg/m2 to 115 mg/m2 with infusion times of 1 to 2 hours.

Docetaxel's pharmacokinetic profile is consistent with a three-compartment pharmacokinetic model, with half-lives for the phases of 4 min, 36 min, and 11.1 hr, respectively. The mean total body clearance is 21 L/h/m2.

Distribution
Docetaxel initially gets distributed to the peripheral compartments and the late (terminal) phase is due, in part, to a relatively slow efflux of docetaxel from the peripheral compartment. The mean steady-state volume of distribution is 113 L.

Docetaxel is about 94% protein bound, mainly to 1-acid glycoprotein, albumin, and lipoproteins.

Metabolism
Docetaxel gets metabolized by the CYP3A4 isoenzyme, and its metabolism may be modified by the concomitant administration of compounds that induce, inhibit, or are metabolized by cytochrome P450 3A4.

Elimination
Docetaxel gets eliminated in both the urine and faeces following oxidative metabolism of the tertiary-butyl ester group, but faecal excretion is the main elimination route. About 80% is excreted during the first 48 hours as 1 major and 3 minor metabolites with very small amounts (less than 8%) of unchanged drug.

5.3 Preclinical safety data
The carcinogenic potential of docetaxel has not been studied.

Docetaxel has been shown to be mutagenic in the in vitro micronucleus and chromosome aberration test in CHO-K1 cells and in the in vivo micronucleus test in the mouse. However, it did not induce mutagenicity in the Ames test or the CHO/HGPRT gene mutation assay. These results are consistent with the pharmacological activity of docetaxel.

Undesirable effects on the testis observed in rodent toxicity studies suggest that docetaxel may impair male fertility.

6. Pharmaceutical particulars

6.1 List of excipients
Polysorbate 80
Citric acid

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
24 months.

6.4 Special precautions for storage
Store below 2°C and 8°C. Protect from light.

6.5 Nature and contents of the container
A flint USP type I glass vial closed with a 20mm grey bromo butyl rubber stopper with an aluminium seal.

CP-Docetaxel 20
Fill volume: 0.5 mL.
Pack size: 1 vial.

CP-Docetaxel 80
Fill volume: 1 mL.
Pack size: 1 vial.

CP-Docetaxel 120
Fill volume: 3 mL.
Pack size: 1 vial.

6.6 Special precautions for disposal and other handling
Docetaxel is a cytotoxic anticancer drug and as with other potentially toxic compounds, caution should be exercised when handling and preparing Docetaxel solutions. The use of gloves is recommended. If docetaxel concentrate, premix solution, or infusion comes into contact with skin or mucosa immediately and thoroughly wash with soap and water. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. APPLICANT
Cospharm Investments Pvt.Limited
Erf 492 Dante Street Prosperita
Windhoek
Namibia

8. MANUFACTURER
Naprod Life Sciences Pvt. Limited
Factory: G-17/1, M.I.D.C., Tarapur, Boisar
Dist. Thane - 401 506
India

9. REGISTRATION DETAILS
CP-Docetaxel 20
Zimbabwe registration number: 2023/9.4/6476
Zimbabwe category for distribution: Prescription Preparations (P.P.)

CP-Docetaxel 80
Zimbabwe registration number: 2023/9.4/6477
Zimbabwe category for distribution: Prescription Preparations (P.P.)

CP-Docetaxel 120
Zimbabwe registration number: 2023/9.4/6478
Zimbabwe category for distribution: Prescription Preparations (P.P.)

10. DATE OF REVISION OF THE TEXT
November 2023