SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

Docetaxel Injection Concentrate 80 mg

2. Pharmaceutical Form

Pharmaceutical Dosage form of the product: Liquid Injection

Strength: 80 mg /vial

Route(s) of administration: Intravenous route of administration

3. Qualitative and Quantitative Composition

D-Tail
(Docetaxel Injection Concentrate 80 mg)

Composition

Label claim:
Each vial contains:

Docetaxel Trihydrate equivalent to anhydrous Docetaxel	80 mg
Polysorbate 80 BP	qs to 2.0 ml

Sr. No.	Ingredient	Qty in mg/ml	Function
1.	Docetaxel Trihydrate IH equivalent to anhydrous Docetaxel (with 5% overages)	44.8 mg 42.0 mg	Anti-neoplastic
2.	Polysorbate 80 BP	qs 1.0 ml	Solvent
3.	Citric acid Anhydrous BP	16.0 mg	pH adjustment

4. Clinical Particulars

4.1 Therapeutic indications

The preparation shall be indicated in treatment of patients with locally advanced metastatic breast cancer and non-small cell lung cancer.

4.2 Posology and method of administration

DOSAGE:

D-TAIL should be administered by intravenous infusion only.

The recommended dosage of **Docetaxel** is 60-100 mg/m^2 administered as a one-hour infusion every three weeks.

DIRECTIONS FOR USE:

Premedication:

In order to reduce adverse reactions like fluid retention, it is recommended that every patient should be premedicated with oral corticosteroids such as Dexamethasone 16 mg per day for 4-5 days starting 1 day before the administration of **Docetaxel.**

Docetaxel should not be administered until the neutrophil count is at least 1500 cell/mm^3. Patients who experience either febrile neutropenia, neutrophil < 500 cell/mm^3 for more than one week, severe or cumulative cutaneous reactions or severe peripheral neuropathy during **Docetaxel** therapy should have the dosage of **Docetaxel** reduced from 100 mg/m^2 to 75 mg/m^2. If the patient continues to experience these reactions at 75 mg/m^2, the dosage should be decreased from 75 mg/m^2 to 55mg/m^2.

Handling and Disposal:

Standard procedures for proper handling and disposal of anti-cancer drugs should be considered. Several guidelines have been issued but there is no general agreement that all the procedures are necessary or appropriate. However, the following general procedure may be adopted.

Docetaxel is a potential toxic compound and caution should be exercised while handling it and preparing **Docetaxel** solution.

Use of protective gloves and clothing is recommended and only an expert should reconstitute the agent.

In the event of the **Docetaxel** concentrate, premix solution or infusion solution coming in direct contact with the skin, the skin should be washed immediately with soap and water. If they come into direct contact with eye or sensitive mucous membrane they should be washed immediately and thoroughly with water.

Adequate precautions and care should be taken while disposing off the items used to reconstitute the solution.

PREPARATION FOR THE INTRAVENOUS ADMINISTRATION:

a) Preparation of D-TAIL premix solution:

Take out required number of vials of D-TAIL from the refrigerator and

allow them to stand for 5 minutes to bring it to room temperature. Withdraw the entire contents of the Solvent vial into a syringe and transfer aseptically to the vial of D-TAIL. Shake the vial for 15 seconds by manual rotation and then allow this D-TAIL premix solution to stand for 5 minutes at room temperature. The solution should be clear and homogenous. There may be foaming which is due to Polysorbate 80 BP. The D-TAIL premix solution contains 10 mg Docetaxel/ml.

b) Preparation of the infusion solution:

Withdraw aseptically the required amount of D-TAIL premix solution with a calibrated syringe and inject the premix volume into an infusion bag or bottle of either 0.9% Sodium Chloride Injection or 5% Dextrose Injection to produce a final concentration of 0.3 to 0.9 mg of Docetaxel/ml The infusion solution should then be thoroughly mixed by manual rotation.

Administer intravenously Docetaxel infusion solution as a one hour infusion under room temperature and normal lighting conditions.

Do not admix with other medications.

Docetaxel infusion is compatible with commonly available IV administration sets including PVC sets

4.3 Method of administration

Intravenous Route of Administration

4.4 Contraindications

History of hypersensitivity reactions to **Docetaxel** or Polysorbate 80.

Patients with baseline neutrophil count of < 1500 cells/mm^3

4.5 Special warning & precautions for use

Docetaxel (D-TAIL) should be administered under supervision of a physician experienced in the use of cancer chemotherapeutic agents. Since significant hypersensitivity reactions may occur, appropriate management of complications is possible only when adequate diagnostic and treatment facilities are readily available. During the infusion, it is recommended that vital functions should be closely monitored.

In order to reduce the fluid retention all the patients should be premedicated with oral corticosteroids like Dexamethasone 16 mg per day for 4-5 days beginning 1 day prior to Docetaxel administration.

Patients should be treated with Docetaxel only when baseline neutrophil count is > 1500/mm^3. Frequent monitoring of complete blood count should be performed regularly during Docetaxel therapy. The subsequent dose of Docetaxel should be reduced in case of Grade IV neutropenia (neutrophil Count<500/mm^3) lasting for 7 days or more.

Hypersensitivity reaction (HSR) may occur within a few minutes following the initiation of the infusion of Docetaxel. Minor HSR may manifest as mild flushing or localized skin reactions however interruption

of therapy is not required in such cases. Severe HSRs such as hypotension (reduction of blood pressure by more than 20 mm Hg) or bronchospasm or generalized rashes require immediate cessation of infusion and aggressive symptomatic therapy. Patients who have developed severe HSRs should not be rechallenged with Docetaxel.

Peripheral neuropathy may be observed in a few patients during D-TAIL therapy. Subsequent dose reduction is suggested in case of peripheral neuropathy.

Safety of Docetaxel has not been established in children; hence a cautious use is suggested utilizing risk vs. benefit ratio.

As Safety of Docetaxel has not been established in pregnancy and lactation, the women with child bearing age should avoid pregnancy.

Skin reactions such as localized skin erythema of the extremities (palm of the hand and sole of the feet) with oedema followed by desquamation have been reported with Docetaxel therapy. This type of toxicity can lead to interruption or discontinuation therapy.

4.6 Interaction with other medicinal products and other forms of interactions

Adequate precaution should be taken while administering Docetaxel and Ketoconazole, as in vitro studies have shown that an interaction occurs between Ketoconazole and Docetaxel.

4.7 Pregnancy and lactation

4.8 Effects on ability to drive and use machine

Not known.

4.9 Undesirable effects

The following side effects have been reported from several clinical trials on Docetaxel.

Bone Marrow Suppression*:*

Usually mild but in some cases severe neutropenia (neutrophils <500 cell/m^2) has been reported. This is non-cumulative and reversible. Neutropenic fever and anaemia have also been reported. Severe thrombocytopenia has been reported in a few patients.

Hypersensitivity Reactions:

Mild hypersensitivity reactions such as flushing. Tightness in the chest, rashes, pruritis, mild dyspnea, or chills may occur.

Severe hypersensitivity reactions in the form of hypotension (fall in B.P. by more than 20 mm Hg) and bronchospasm may occur. This may require discontinuation of therapy and aggressive symptomatic treatment.

Fluid retention:

Gain of body weight by more than 3 kg has been reported after 4 or more

cycles or after a cumulative dose of = 400 mg/m^2 as a result of fluid retention. Fluid retention in the form of oedema, pleural effusion, ascites and increased capillary permeability has been reported. Discontinuation of Docetaxel treatment causes slow reversal of this fluid retention.
Premedication with oral corticosteroids has been observed to reduce the fluid retention.

Skin Reaction*:*
Skin reaction has been observed in the form of rash, localized eruptions mainly on feet, hands, arms, face and chest and are often associated with itching. Usually these reactions occur within a week of Docetaxel infusion and recover before the next infusion. Rarely severe symptoms such as desquamation may occur. Nails have also been reported to exhibit symptoms of toxicity as hyper pigmentation, pain and oncholysis.
Gastrointestinal effects such as nausea, vomiting or diarrhea may occur.
Neurotoxicity has been reported during the clinical trials conducted abroad.
Cardiovascular events of clinical meaning occurred rarely.
Other undesirable effects have included alopecia, asthenia, mucositis, and arthralgias.

4.10 Overdose

There is no known antidote for Docetaxel overdose. The known complication of overdose included neutropenia, cutaneous reactions and sensory neuropathy. The patient should be kept in specialized unit and vital functions should be closely monitored in such case of overdose and myalgias, hypotension and injection site reactions.

5. Pharmacological Properties

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Antineoplastic Agents

ATC Code: L01CD02

Docetaxel is an antineoplastic agent acting at the microtubules. **Docetaxel** enhances polymerization of the tubulin into stable microtubules and inhibits their depolymerisation. This induces the formation of stable microtubules bundles leading to cell death.

5.2 Pharmacokinetic Properties

The pharmacokinetic studies on **Docetaxel** reveal that there is no schedule dependence of **Docetaxel** disposition. The AUC increase in proportion to the dose of **Docetaxel** administered, from 0.96 µg.h/ml (20 mg/m^2) to 5.2 µg.h/ml (115mg/m^2) consistent with linear pharmacokinetics. At the highest clinical dose levels examined in the 1-h infusion schedule every 3 weeks. **Docetaxel** disposition was triphasic, with a terminal half-life of 11 to 18 h and plasma of 16 to 21 l/h/m^2. Following the administration of 70-100 mg dose given as a 1-2 hour infusion, the peak plasma level of 3.8 µg/ml was obtained with a corresponding AUC of 4.7 h.µg/ml. The half-lives for a, ß and γ phases were 5 min, 36 min and 12.2 hours respectively while systemic clearance was 21 l/h/m^2.

The major route of elimination of **Docetaxel** and its metabolite is fecal which about 80% of the drug is excreted. About 5% excretion takes place through urine. Only a minor fraction of administered drug is excreted as the parent drug. **Docetaxel** metabolism involves the isoenzymes of the cytochrome P450-3A subfamily and more than 95% of **Docetaxel** is bound to plasma proteins.

5.3 Preclinical safety data

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6. Pharmaceutical Particulars

6.1 List of Excipients

Citric Acid Anhydrous BP
Polysorbate 80 BP

6.2 Incompatibilities

None

6.3 Shelf life

The shelf life of the medicinal product as package for sale
24 Months

The shelf life after dilution or reconstitution according to directions
Not Applicable.

The shelf life after first opening the container
Not Applicable

6.4 Special precaution for storage

Store between 2°C-8°C. Protect from light.

6.5 Nature and contents of container

UNIT PACK: 10 ml flint moulded Glass Type I vial, closed with 20 mm slotted grey bromobutyl rubber stopper and sealed with yellow coloured aluminium flip off seal, packed in a printed carton along with a pack insert.

7. Marketing Authorization Holder and Manufacturing site address

Name of Marketing Authorization Holder:
Khandelwal Laboratories Pvt. Ltd.

Address of manufacturing site:
B-1, Wagle Industrial Estate,
Thane - 400 604, India
Telephone: 00 91 22 25821793 / 0794
Fax: 00 91 22 25823837

8. Marketing Authorization Numbers

06318/06771/NMR/2018

9. Date of first authorization / renewal of the authorization

Jul 25, 2021

10. Date of revision of the text

Jul 25, 2021