

SCHEDULING STATUS:	
S4:	CIPLA-DOCETAXEL 20 CIPLA-DOCETAXEL 80
S1:	SOLVENT FOR CIPLA-DOCETAXEL 20 INJECTION SOLVENT FOR CIPLA-DOCETAXEL 80 INJECTION

PROPRIETARY NAME (AND DOSAGE FORM):

CIPLA-DOCETAXEL 20 (Solution for infusion)

CIPLA-DOCETAXEL 80 (Solution for infusion)

SOLVENT FOR CIPLA-DOCETAXEL 20 INJECTION (Solvent)

SOLVENT FOR CIPLA-DOCETAXEL 80 INJECTION (Solvent)

COMPOSITION:	
CIPLA-DOCETAXEL 20:	Each single-dose vial contains docetaxel trihydrate equivalent to 20 mg docetaxel (anhydrous) in 0.5 ml polysorbate 80.
CIPLA-DOCETAXEL 80:	Each single-dose vial contains docetaxel trihydrate equivalent to 80 mg docetaxel (anhydrous) in 2,0 ml polysorbate 80.

SOLVENT FOR CIPLA-DOCETAXEL 20 INJECTION:	Each vial contains 13.0 % m/v ethanol 95 % v/v.
SOLVENT FOR CIPLA-DOCETAXEL 80 INJECTION:	Each vial contains 13.0 % m/v ethanol 95 % v/v.

PHARMACOLOGICAL CLASSIFICATION:
A 26 Cytostatic agents.
A.32.2 Other

PHARMACOLOGICAL ACTION:

Pharmacodynamics:
Docetaxel, an antineoplastic agent, promotes the assembly of tubulin into stable microtubules and inhibits their disassembly. This causes a marked decrease in free tubulin. The binding of docetaxel to microtubules does not change the number of protofilaments.

It has been shown *in vitro* that docetaxel disrupts the microtubular network in cells, which is crucial for vital mitotic and interphase cellular functions. Docetaxel reaches high intracellular concentrations with a long cell residence time. In addition, it has been shown that docetaxel is active against some, but not all, cell lines over-expressing the paralogousprotein which is encoded by the multidrug resistance gene. *In vivo*, docetaxel is not schedule-dependant.

Pharmacokinetics:
Docetaxel displays a dose-independent kinetic profile which is consistent with a three-compartment pharmacokinetic model. The half-lives for the alpha, beta and gamma phases are 4 minutes, 36 minutes and 11,1 hours, respectively. The late phase results, in part, from a relatively slow efflux of docetaxel from the peripheral compartment. The administration of a 100 mg/m² dose infused over one hour results in a mean peak plasma level of 3,7 µg/ml with a corresponding AUC of 4,6 h.µg/ml. Mean total body clearance is 21 L/h/m² and mean steady-state volume of distribution is 113 L. Plasma protein binding is in excess of 95 %.

Docetaxel and its metabolites are mainly excreted via the faecal route with faecal and urinary excretions accounting for approximately 75 % and 6 % of the dose, respectively.

Faecal excretion is the main route of elimination of docetaxel and its metabolites. Faecal and urinary excretion account for about 75 % and 6 % of the dose, respectively. Only a minor portion of the dose is excreted as the parent compound. *In vitro* studies have indicated that isoenzymes of the cytochrome P450 3A subfamily are involved in the metabolism of docetaxel.

INDICATIONS:

1. **Breast cancer:**

The combination of **CIPLA-DOCETAXEL**, doxorubicin and cyclophosphamide is indicated for the adjuvant treatment of females with surgically resectable node-positive breast cancer.

The combination of **CIPLA-DOCETAXEL** and doxorubicin is indicated for the treatment of patients with locally advanced or metastatic breast cancer in the absence of a history of previous cytotoxic therapy for this condition.

CIPLA-DOCETAXEL single agent therapy is indicated for the treatment of patients with locally advanced or metastatic breast cancer who have failed to respond to cytotoxic therapy.

CIPLA-DOCETAXEL, in combination with capecitabine, is indicated for the treatment of patients with locally advanced or metastatic breast cancer who have failed treatment with cytotoxic chemotherapy in which instance previous therapy should have included an anthracycline.

2. **Non-small cell lung cancer:**

CIPLA-DOCETAXEL, combined with cisplatin, is indicated for the treatment of patients with non-resectable, locally advanced or metastatic non-small cell lung cancer, with no history of previous chemotherapy for this condition.

CIPLA-DOCETAXEL is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer, even if they previously failed to respond to platinum-based chemotherapy.

3. **Ovarian cancer:**

CIPLA-DOCETAXEL is indicated, after failure of first-line or subsequent chemotherapy, for the treatment of patients with metastatic ovarian carcinoma.

4. **Prostate cancer:**

CIPLA-DOCETAXEL, in combination with prednisone or prednisolone, is indicated for the treatment of men with androgen-independent (hormone-refractory) metastatic carcinoma of the prostate.

5. **Cancer of the head and neck:**

CIPLA-DOCETAXEL, in combination with cisplatin and 5-fluorouracil, is indicated for the induction treatment of individuals with inoperable squamous cell carcinomas of the head and neck that are locally advanced.

CONTRA-INDICATIONS:

CIPLA-DOCETAXEL is contra-indicated in:

- Patients who have a history of hypersensitivity reactions to docetaxel or polysorbate 80.
- Patients with baseline neutrophil count of < 1500 cells/mm³.
- Pregnancy and lactation as teratogenicity has been shown in animals.
- Children as safety has not been established.
- Patients with severe liver impairment since there are no data available (see "**WARNINGS**" and "**DOSAGE AND DIRECTIONS FOR USE**").

Contra-indications for other medicines also apply when used in combination with **CIPLA-DOCETAXEL**.
WARNINGS:

Patients should receive **CIPLA-DOCETAXEL** under the supervision of a qualified physician experienced in the use of antineoplastic agents. It is only possible to appropriately manage complications when adequate diagnostic and treatment facilities are readily available.

Abnormal liver function and higher doses increase the incidence of treatment-related mortality associated with **CIPLA-DOCETAXEL**.

As a general rule, **CIPLA-DOCETAXEL** should not be administered to patients with serum bilirubin levels > upper limit of normal (ULN), or to patients with AST and/or ALT > 1,5 x ULN concomitant with alkaline phosphatase levels > 2,5 x ULN. Patients with elevated bilirubin levels or abnormalities of transaminases in conjunction with alkaline phosphatase are at increased risk of experiencing grade 4 neutropenia, febrile neutropenia, infections, sever thrombocytopenia, severe stomatitis, severe skin toxicity and toxic death.

Patients with isolated transaminase elevations > 1,5 x ULN also demonstrated a higher rate of febrile neutropenia grade 4, but did not show an increased incidence of toxic death. Bilirubin, AST or ALT and alkaline phosphatase values should be determined before each cycle of **CIPLA-DOCETAXEL** therapy and reviewed by the treating physician.

CIPLA-DOCETAXEL should not be administered to patients with neutrophil counts of < 1500 cells/mm³. In order to monitor the development of neutropenia, which may be severe and result in infection, frequent blood cell counts should be obtained in all patients receiving treatment with **CIPLA-DOCETAXEL**.

Severe hypersensitivity reactions characterised by hypotension and/or bronchospasm or generalised rash/erythema developed in 2,2 % of patients given the recommended 3-day dexamethasone premedication. Hypersensitivity reactions requiring cessation of therapy with **CIPLA-DOCETAXEL** were observed in some patients who did not receive premedication. Such reactions resolved after cessation of the infusion and the administration of appropriate therapy.

CIPLA-DOCETAXEL must not be administered to patients who previously experienced severe hypersensitivity reactions to **CIPLA-DOCETAXEL** or to other medicines formulated with polysorbate 80.

Despite use of a 3-day dexamethasone premedication regimen, severe fluid retention developed in 6,5 % of patients. This development was characterised by one or more of the following: poorly tolerated peripheral oedema, generalised oedema, pleural effusion requiring urgent drainage, dyspnoea at rest, cardiac tamponade or pronounced abdominal distension (due to ascites).

Please note: Contact of the **CIPLA-DOCETAXEL** concentrate with plasticised PVC equipment or devices used to prepare solutions for infusion is not recommended. In order to minimise patient exposure to the plasticiser DEHP (di-2-ethylhexyl phthalate), which may be leached from PVC infusion bags or sets, the final **CIPLA-DOCETAXEL** dilution for infusion should be stored in bottles (glass, polypropylene) or plastic bags (polypropylene, polyolefin) and administered through polyethylene-lined administration sets (see "**DOSAGE AND DIRECTIONS FOR USE**").

The administration of **CIPLA-DOCETAXEL** should be confined to units specialised in the use of cytotoxic chemotherapy. **CIPLA-DOCETAXEL** should only be given under the supervision of a qualified oncologist. Since significant hypersensitivity reactions may develop, appropriate supportive equipment should be available. It is advised that vital functions should be closely monitored during the infusion.

Premedication with an orally administered corticosteroid (see below for prostate), such as dexamethasone 16 mg per day (e.g. 8 mg twice daily) for 3 days, unless contra-indicated, may reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions. Such premedication should be given one day prior to the administration of **CIPLA-DOCETAXEL**. For patients with prostate cancer the pretreatment regimen is 8 mg oral dexamethasone administered 12 hours, 3 hours and 1 hour before the **CIPLA-DOCETAXEL** regimen.

Haematology:

The most frequent adverse reaction due to **CIPLA-DOCETAXEL** is neutropenia which develops in almost all patients. Severe neutropenia (grade 3 – 4) developed in 99 % of patients who received combination therapy with doxorubicin.

Neutrophil nadirs occurred at a median of 7 days, although this interval may be shorter in patients who were heavily pretreated. Complete blood cell counts should be frequently performed in all patients receiving **CIPLA-DOCETAXEL**. Patients should receive further treatment with **CIPLA-DOCETAXEL** only after neutrophil counts recover to a level ≥ 1500 cells/mm³ (see "**DOSAGE AND DIRECTIONS FOR USE**").

Should severe neutropenia (< 500 cells/mm³ for seven days or more) develop during a course of **CIPLA-DOCETAXEL** therapy, a reduction in dose for subsequent cycles of therapy and the use of appropriate symptomatic measures are advised.

Hypersensitivity reactions:

Patients require close observation for hypersensitivity reactions, especially during the first and second infusions. Hypersensitivity reactions may develop within a few minutes following the start of the **CIPLA-DOCETAXEL** infusion; therefore facilities for the treatment of hypotension and bronchospasm should be available. If hypersensitivity reactions develop, minor symptoms, such as flushing or localised cutaneous reactions do not call for the interruption of therapy. However, should more severe reactions occur, such as hypotension with a reduction of more than 20 mm Hg, bronchospasm or generalised rash/erythema, the infusion should be immediately discontinued and appropriate symptomatic therapy instituted.

Patients who experienced severe hypersensitivity reactions should not be rechallenged with **CIPLA-DOCETAXEL**.

Fluid retention:

Premedication with a corticosteroid, such as oral dexamethasone 16 mg per day (e.g. 8 mg twice daily) for 3 days, initiated one day prior to **CIPLA-DOCETAXEL** administration, may lower the incidence and reduce the severity of fluid retention as well as the severity of hypersensitivity reactions.

Patients with severe fluid retention, such as pleural effusion, pericardial effusion and ascites, require close monitoring.

Liver impairment:

Patients who receive **CIPLA-DOCETAXEL** at 100 mg/m² who have serum transaminase levels (ALT and/or AST) greater than 1,5 times the upper limit of normal (ULN) in combination with serum alkaline phosphatase levels greater than 2,5 times ULN, have a higher risk of experiencing severe adverse reactions, such as toxic deaths, including sepsis and gastrointestinal haemorrhage which can be fatal, febrile neutropenia, infections, thrombocytopenia, stomatitis and asthma. The recommended dose of **CIPLA-DOCETAXEL** in patients with elevated liver function tests (LFTs) is therefore 75 mg/m² and LFTs should be determined at baseline and prior to each cycle (see "**DOSAGE AND DIRECTIONS FOR USE**"). For patients with serum bilirubin levels > ULN and/or ALT and AST > 3,5 times ULN combined with serum alkaline phosphatase levels ≥ 6 times ULN, no dose reduction can be recommended and **CIPLA-DOCETAXEL** should not be given unless strictly indicated.

Cutaneous reactions:

Localised skin erythema of the extremities (palms of the hands and soles of the feet) with oedema followed by desquamation may develop. This type of toxicity may necessitate the interruption or cessation of treatment.

Nervous system:

Severe peripheral neurotoxicity, including paraesthesia, dysaesthesia and pain, has been observed and requires a dose reduction. If symptoms persist, treatment should be discontinued.

Elderly:

An analysis of safety data in patients 60 years of age and older who received **CIPLA-DOCETAXEL** and capecitabine combination therapy revealed an increase in the incidence of treatment-related grade 3 and 4 adverse events, treatment-related serious adverse events and early withdrawals from treatment due to adverse events compared to patients less than 60 years of age. Patients who were 65 years of age who received **CIPLA-DOCETAXEL** every three weeks had > 10 % higher incidence rates of anaemia, infection, nail changes, anorexia, and weight loss.

Others:
Contraceptive measures must be taken during and for at least three months after discontinuation of **CIPLA-DOCETAXEL** treatment.

INTERACTIONS:

There is a paucity of formal clinical studies that evaluated drug interactions due to **CIPLA-DOCETAXEL**.

In vitro studies have demonstrated that the metabolism of **CIPLA-DOCETAXEL** may be modified by the concurrent administration of compounds which induce, inhibit or are metabolised by (and thus may inhibit the enzyme competitively) cytochrome P450-3A, such as ciclosporin, ketoconazole, erythromycin and troleanomycin. As a result, caution is required when patients are concomitantly treated with these agents, since there is potential for significant interactions.

CIPLA-DOCETAXEL is highly bound to plasma proteins (> 95 %). Although the possible *in vivo* interaction of **CIPLA-DOCETAXEL** with concurrently administered medicines has not been studied formally, *in vitro* interactions with lightly protein-bound medicines, such as erythromycin, diphendramine, propranolol, propafenone, phenytoin, salicylate, sulphamethoxazole and sodium valproate did not influence protein binding of docetaxel. In addition, dexamethasone did not influence protein binding of **CIPLA-DOCETAXEL**.

CIPLA-DOCETAXEL does not affect the protein binding of digoxin.

When used concurrently with doxorubicin, **CIPLA-DOCETAXEL** does not affect the clearance of doxorubicin nor the plasma levels of doxorubicinol (a doxorubicin metabolite). However, **CIPLA-DOCETAXEL** clearance was increased.

CIPLA-DOCETAXEL clearance when administered in combination with cisplatin is similar to that observed following monotherapy. The pharmacokinetic characteristics of cisplatin given shortly after **CIPLA-DOCETAXEL** infusion are similar to that seen with cisplatin alone. Capecitabine does not affect the pharmacokinetics of **CIPLA-DOCETAXEL** (C_{max} and AUC) and

CIPLA-DOCETAXEL does not have any effect on the pharmacokinetics of the main capecitabine metabolite 5'-DFUR.

Prednisone does not affect **CIPLA-DOCETAXEL** pharmacokinetics.

Caution is required when **CIPLA-DOCETAXEL** is administered to patients who are concomitantly receiving potent CYP3A4 inhibitors (e.g. protease inhibitors like ritonavir and azole antifungals like ketoconazole or itraconazole). A medicine interactions study performed in patients receiving ketoconazole and docetaxel, as in **CIPLA-DOCETAXEL**, demonstrated that ketoconazole reduces docetaxel clearance by half, probably because docetaxel metabolism involves CYP3A4 as a major (single) metabolic pathway. Patients may demonstrate reduced tolerance to **CIPLA-DOCETAXEL**, even at lower doses.

PREGNANCY AND LACTATION:

Pregnancy and lactation are contra-indications to the use of **CIPLA-DOCETAXEL**, as **CIPLA-DOCETAXEL** is teratogenic in animals (see "**CONTRA-INDICATIONS**" and "**WARNINGS**").

DOSAGE AND DIRECTIONS FOR USE:

Patients should receive **CIPLA-DOCETAXEL** by intravenous infusion only.

Dosage:

A corticosteroid premedication (see below for prostate cancer), such as oral dexamethasone 16 mg per day (e.g. 8 mg twice daily) for 3 days, unless contra-indicated, can be given. This should be initiated one day prior to **CIPLA-DOCETAXEL** administration. For prostate cancer, in view of the concomitant use of prednisone or prednisolone, the recommended premedication regimen is oral dexamethasone 8 mg given 12 hours, 3 hours and 1 hour prior to the **CIPLA-DOCETAXEL** infusion.

G-CSF may be administered prophylactically to moderate the risk of haematological toxicities.

CIPLA-DOCETAXEL is infused over a period of one hour every three weeks.

1. **Breast cancer:**

In the adjuvant treatment of surgically resectable node-positive breast cancer, the recommended **CIPLA-DOCETAXEL** dose is 75 mg/m² infused one hour after doxorubicin 50 mg/m² and cyclophosphamide 500 mg/m² every 3 weeks for 6 cycles (see also "**Dosage adjustments during therapy**").

In first-line treatment, **CIPLA-DOCETAXEL** 75 mg/m² is given in combination with doxorubicin (50 mg/m²).

For second-line monotherapy for patients who previously received treatment, the recommended dosage of **CIPLA-DOCETAXEL** therapy is 100 mg/m² in monotherapy.

When used in combination with capecitabine, the recommended dose of **CIPLA-DOCETAXEL** is 75 mg/m² every three weeks, concomitantly with capecitabine 1250 mg/m² orally twice daily with 30 minutes after a meal) for 2 weeks followed by a 1-week rest period. Please consult capecitabine manufacturer's prescribing information for capecitabine dose calculation according to body surface area.

2. **Non-small cell lung cancer:**

In combination therapy (chemotherapy-naïve patients):
The recommended dosage regimen is **CIPLA-DOCETAXEL** 75 mg/m² following which cisplatin 75 mg/m² over 30 – 60 minutes should be administered immediately.

In monotherapy (for previously treated patients):

The recommended **CIPLA-DOCETAXEL** dosage is 100 mg/m² as a single agent.

3. **Ovarian cancer:**

The recommended **CIPLA-DOCETAXEL** dosage is 100 mg/m².

4. **Prostate cancer:**

The recommended **CIPLA-DOCETAXEL** dose is 75 mg/m². Patients should continuously receive prednisone or prednisolone 5 mg orally twice daily.

Patients require close observation, especially during the first and second infusion of **CIPLA-DOCETAXEL**, due to the risk of hypersensitivity reactions.

5. **Head and neck cancer:**

For the induction treatment of locally advanced inoperable squamous cell carcinoma of the head and neck (SCCHN), the recommended dose of **CIPLA-DOCETAXEL** is 75 mg/m² infused over 1 hour. This should be followed by cisplatin 75 mg/m² administered over 1 hour, on day one, followed by 5-fluorouracil given as a continuous infusion at a dose of 750 mg/m² per day for five days. Patients should receive this regimen every two weeks for 4 cycles. After chemotherapy, patients should be given radiotherapy. Patients require premedication with anti-emetics and appropriate hydration (before and after cisplatin administration). Patients also require prophylaxis for neutropenic infections. For cisplatin and 5-fluorouracil dose modifications, see their respective package inserts.

Dosage adjustments during treatment:

General:

ONLY the treating oncologist can modify the schedule of administration.

Patients should receive **CIPLA-DOCETAXEL** when the neutrophil count is ≥ 1500 cells/mm³. Patients who developed either febrile neutropenia, neutrophil count < 500 cells/mm³ for more than one week, severe or cumulative cutaneous reactions or severe neurosensory signs and/or symptoms during treatment with **CIPLA-DOCETAXEL**, should have their **CIPLA-DOCETAXEL** dosage reduced during the subsequent cycle, from 100 mg/m² to 75 mg/m² and/or from 75 mg/m² to 60 mg/m². If the patient continues to experience these adverse events at 60 mg/m², treatment should be stopped.

Combination therapy with CIPLA-DOCETAXEL for non-small cell lung cancer:

For patients who initially received **CIPLA-DOCETAXEL** at 75 mg/m² in combination with cisplatin, and whose nadir of platelet count during the previous course of therapy was < 25000 cells/mm³, or in patients who develop febrile neutropenia, or in patients with serious non-haematological toxicities, the **CIPLA-DOCETAXEL** dosage requires reduction in subsequent cycles to 65 mg/m². For adjustments to the cisplatin dosage, see the manufacturer's prescribing information.

Combination therapy with CIPLA-DOCETAXEL for breast cancer:

Patients who receive adjuvant therapy for breast cancer and who develop febrile neutropenia should be given G-CSF in all subsequent cycles. Should patients continue to experience this adverse event, they should remain on G-CSF and have their **CIPLA-DOCETAXEL** dose reduced to 60 mg/m². If G-CSF is not given, the **CIPLA-DOCETAXEL** dose requires reduction from 75 to 60 mg/m².

For capecitabine dose modifications when used in combination with **CIPLA-DOCETAXEL**, consult capecitabine manufacturer's prescribing information.

For patients experiencing the first appearance of grade 2 toxicity which persists at the time of the next **CIPLA-DOCETAXEL**/capecitabine administration, postpone treatment until resolved to grade 0 – 1, and resume at 100 % of the original dose. For patients experiencing the second appearance of grade 2 toxicity, or the first appearance of grade 3 toxicity, at any time during the course of treatment, postpone treatment until resolved to grade 0 – 1, then resume treatment with **CIPLA-DOCETAXEL** 55 mg/m². In the event of any subsequent appearances of toxicities, or any grade 4 toxicities, discontinue **CIPLA-DOCETAXEL**.

For **CIPLA-DOCETAXEL** dose adjustments due to liver impairment, see "**WARNINGS**" and "**Special populations**".

Special populations:

Patients with hepatic impairment:

CIPLA-DOCETAXEL should generally not be administered to patients with bilirubin > ULN. **CIPLA-DOCETAXEL** should also generally not be given to patients with AST and/or ALT > 1,5 x ULN concomitant with alkaline phosphatase > 2,5 x ULN.

Children:

It has not been established whether **CIPLA-DOCETAXEL** is safe and effective when used in children (see "**CONTRA-INDICATIONS**").

Elderly:

Based on a population pharmacokinetic analysis, there are no special instructions for **CIPLA-DOCETAXEL** when administered to the elderly.

For capecitabine dosage reduction when administered in combination with **CIPLA-DOCETAXEL**, see capecitabine manufacturer's prescribing information.

Recommendations for safe handling:

Handling precautions for cytostatic medicines should be adhered to:

- Only trained staff should reconstitute the medicine in a designated area.
- CIPLA-DOCETAXEL** is an antineoplastic agent and, similar to other potentially toxic compounds, caution is required when handling it and preparing **CIPLA-DOCETAXEL** solutions.
- Disposable plastic-backed absorbent paper should be placed over the work surface.
- It is necessary to wear adequate protective gloves and clothing.
- If **CIPLA-DOCETAXEL** concentrate, premix solution or infusion solution should come into contact with the skin, use soap and water to wash immediately and thoroughly. If **CIPLA-DOCETAXEL** concentrate, premix solution or infusion solution should come into contact with the eyes or mucous membranes, use water to wash immediately and thoroughly.
- Pregnant staff should not handle the cytotoxic preparation.
- Adequate care and precautions are required in the disposal of items used to reconstitute this medicine.

Directions for use:

CIPLA-DOCETAXEL 20 mg vial and CIPLA-DOCETAXEL solvent vial:

Each **CIPLA-DOCETAXEL** 20 mg vial contains 20 mg of **CIPLA-DOCETAXEL** per 0,5 ml of polysorbate 80 (fill volume: 24,4 mg /0,61 ml).

Each **CIPLA-DOCETAXEL** solvent vial for **CIPLA-DOCETAXEL** 20 mg contains 1,5 ml solvent (fill volume: 1,98 ml).

CIPLA-DOCETAXEL 80 mg vial and CIPLA-DOCETAXEL solvent vial:

Each **CIPLA-DOCETAXEL** 80 mg vial contains 80 mg **CIPLA-DOCETAXEL** per 2 ml of polysorbate 80 (fill volume: 94,4 mg /2,36 ml).

Each **CIPLA-DOCETAXEL** solvent vial for **CIPLA-DOCETAXEL** 80 mg contains 6 ml solvent (fill volume: 7,33 ml).

Preparation for intravenous administration:

a) **Preparation of the CIPLA-DOCETAXEL premix solution (10 mg CIPLA-DOCETAXEL/ml):**

If the vials have been refrigerated, allow the required number of **CIPLA-DOCETAXEL** boxes to stand at room temperature for 5 minutes.

Aseptically withdraw the entire contents of the **CIPLA-DOCETAXEL** solvent vial by partially inverting the vial and using a syringe fitted with a needle.

Empty the syringe by injecting its entire contents into the corresponding **CIPLA-DOCETAXEL** vial.

Remove the syringe and needle and manually mix the contents in the **CIPLA-DOCETAXEL** vial by repeatedly inverting the vial for a minimum of 45 seconds. Do not shake the vial.

Permit this premix vial to stand for 5 minutes at room temperature. The solution should appear homogenous and clear. Due to the presence of polysorbate 80 in the formulation, foaming, which is normal, may be present, even after 5 minutes. This premix solution contains 10 mg/ml **CIPLA-DOCETAXEL**. It should be used immediately to prepare the solution for infusion. It is, however, stable for a maximum of 8 hours provided it is kept at room temperature or in the refrigerator.

b) **Preparation of the infusion solution:**

To obtain the required dose, it may be necessary to use more than one premix vial. Use graduated syringes fitted with needles to aseptically withdraw the required amount of premix solution from the appropriate number of premix vials based on the required dose for the patient expressed in mg. For instance, a dose of 150 mg **CIPLA-DOCETAXEL** would require 15 ml **CIPLA-DOCETAXEL** premix solution.

Inject the required premix volume into