PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1 NAME OF THE MEDICINE

EUROTAX 20 mg Concentrate for solution for infusion

EUROTAX 80 mg Concentrate for solution for infusion

EUROTAX 140 mg Concentrate for solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

EUROTAX 20 mg/1 ml:

Each single-dose vial contains 20 mg docetaxel (anhydrous), in 1 ml of concentrate.

EUROTAX 80 mg/4 ml:

Each single-dose vial contains 80 mg docetaxel (anhydrous), in 4 ml of concentrate.

EUROTAX 140 mg/7 ml:

Each single-dose vial contains 140 mg docetaxel (anhydrous), in 7 ml of concentrate.

Citric acid (anhydrous) – stabilizer and acidifying agent

Ethanol (absolute) – cosolvent for docetaxel and solvent for Kollidon 12PF and anhydrous citric acid.

Povidone (Kollidon 12 PF) – Solubility enhancer for docetaxel

Nitrogen – inert gas used for solution filtration, aseptic filling and vial closing.

Polysorbate 80 (Solvent for docetaxel).

Excipients with known effect:

EUROTAX 20 mg/1 ml:

Each single-dose vial contains 0,42 ml of ethanol (0,4 g)

EUROTAX 80 mg/4 ml:

Each single-dose vial contains 1,68 ml of ethanol (1,6 g)

EUROTAX 140 mg/7 ml:

Each single-dose vial contains 2,95 ml ethanol (2,8 g)

Sugar free.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

EUROTAX concentrate presents as a clear, oily, pale yellow solution in a glass vial.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Breast cancer:

EUROTAX, in combination with doxorubicin and cyclophosphamide, is indicated for the adjuvant treatment of patients with operable node-positive breast cancer.

EUROTAX, in combination with doxorubicin, is indicated for the treatment of patients with locally advanced or metastatic breast cancer who have not previously received cytotoxic therapy for this condition.

EUROTAX monotherapy is indicated for the treatment of patients with locally advanced or metastatic breast cancer, after failure of cytotoxic therapy.

EUROTAX in combination with capecitabine, is indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of cytotoxic chemotherapy. Previous therapy should have included an anthracycline.

Non-small Cell Lung Cancer (NSCLC):

EUROTAX, 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.

EUROTAX is indicated for the treatment of patients with locally advanced or metastatic non small lung cancer, even after failure of platinum-based chemotherapy.

Ovarian Cancer:

EUROTAX is indicated, after failure of first-line or subsequent chemotherapy, for treatment of metastatic carcinoma of the ovary.

Prostate Cancer:

EUROTAX in combination with prednisone or prednisolone, is indicated for the treatment of patients with androgen independent (hormone refractory) metastatic prostate cancer.

Head and Neck Cancer:

EUROTAX in combination with cisplatin and 5-fluorouracil is indicated for the induction treatment of patients with inoperable locally advanced squamous cell carcinoma of the head and neck.

Gastric Adenocarcinoma:

EUROTAX in combination with cisplatin and 5-fluorouracil is indicated for the palliative treatment of patients with advanced gastric adenocarcinoma, including adenocarcinoma of the gastro-oesophageal junction, who have not received prior chemotherapy for advanced disease.

4.2 Posology and method of administration

EUROTAX should be administered by intravenous infusion only.

The use of EUROTAX infusion should be confined to departments specialised in the administration of cytotoxic chemotherapy and it should only be administered under the supervision of a qualified oncologist. Appropriate supportive equipment should be available, and patients should be monitored closely, especially during the first and second infusion of EUROTAX, because of the risk of hypersensitivity reactions.

Posology

A premedication consisting of a corticosteroid (see below for prostate cancer), such as oral dexamethasone 16 mg per day (e.g. 8 mg twice daily) for 3 days, starting one day prior to EUROTAX administration, unless contraindicated, can be used.

For prostate cancer, given the concurrent use of prednisone or prednisolone, the recommended premedication regimen is oral dexamethasone 8 mg, 12 hours, 3 hours and 1 hour before the EUROTAX infusion.

Prophylactic G-CSF may be used to mitigate the risk of haematological toxicities.

EUROTAX is administered as a one-hour infusion every three weeks.

1. Breast Cancer:

In the adjuvant treatment of operable node-positive breast cancer, the recommended dose of EUROTAX is 75 mg/m^2 administered 1-hour after doxorubicin 50 mg/m^2 and cyclophosphamide 500 mg/m^2 every 3 weeks for 6 cycles. (see also “Dosage adjustment during therapy”).

In first-line treatment, EUROTAX 75 mg/m^2 is given in combination therapy with doxorubicin (50 mg/m^2).

For the second-line treatment of breast cancer the recommended dosage of EUROTAX therapy is 100 mg/m^2 in monotherapy.

In combination with capecitabine, the recommended dose of EUROTAX is 75 mg/m^2 every three weeks, combined with capecitabine at 1250 mg/m^2 orally twice daily (within 30 minutes

after a meal) for 2 weeks followed by a 1-week rest period. For capecitabine dose calculation according to body surface area, see capecitabine professional information.

2. Non-small Cell Lung Cancer:

In Combination therapy (chemotherapy naïve patients):

The recommended dosage regimen is EUROTAX 75 mg/m^2 immediately followed by cisplatin 75 mg/m^2 over 30-60 minutes.

In monotherapy (for previously treated patients):

The recommended dosage of EUROTAX is 100 mg/m² as a single medicine.

3. Ovarian Cancer:

The recommended dosage of EUROTAX therapy is 100 mg/m^2.

4. Prostate Cancer:

The recommended dose of EUROTAX is 75 mg/m^2. Prednisone or prednisolone 5 mg orally twice daily is administered continuously.

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 EUROTAX is 75 mg/m^2 as a 1-hour infusion followed by cisplatin 75 mg/m^2 over 1 hour, on day one, followed by 5-fluorouracil as a continuous infusion at 750 mg/m^2 per day for five days. This regimen is administered every 3 weeks for 4 cycles. Following chemotherapy, patients should receive radiotherapy. Patients must receive premedication with antiemetics and appropriate hydration (prior to and after cisplatin administration). Prophylaxis for neutropenic infections should be administered.
For cisplatin and 5-fluorouracil dose modifications, see local professional information.

6. Gastric Adenocarcinoma:

For gastric adenocarcinoma, the recommended dose of EUROTAX is 75 mg/m^2 as a 1-hour infusion, followed by cisplatin 75 mg/m^2, as a 1 to 3 hour infusion (both on day 1 only), followed by 5-fluorouracil 750 mg/m^2 per day given as a 24-hour continuous infusion for 5 days, starting at the end of the cisplatin infusion. Treatment is repeated every three weeks. Patients must receive premedication with anti-emetics and appropriate hydration for cisplatin administration. Prophylactic G-CSF should be used to mitigate the risk of haematological toxicities (see Dosage adjustments during therapy).

Dosage adjustments during treatment:

General:

ONLY the doctor can modify the schedule of administration. EUROTAX should be administered when the neutrophil count is ≥ 1500 cells/mm^3.

Patients who experienced either febrile neutropenia, neutrophil count < 500 cells/mm^3 for more than one week, severe or cumulative cutaneous or severe neurosensory signs and/or symptoms during EUROTAX therapy, should have the dosage of EUROTAX reduced, during the subsequent cycle, from 100 mg/m^2 to 75 mg/m^2 and/or from 75 mg/m^2 to 60 mg/m^2. If the patient continues to experience these reactions at 60 mg/m^2, the treatment should be discontinued.

Combination therapy with EUROTAX for non-small cell lung cancer (NSCLC):

For patients who are dosed initially at EUROTAX 75 mg/m^2 in combination with cisplatin, and whose nadir of platelet count during the previous course of therapy is < 25 000 cells/mm^3, or in patients who experience febrile neutropenia, or in patients with serious non-haematologic toxicities, the EUROTAX dosage in subsequent cycles should be reduced to 65 mg/m^2. For cisplatin dosage adjustments, see professional information.

Combination therapy with EUROTAX for Breast Cancer:

Patients who receive adjuvant therapy for breast cancer and who experience febrile neutropenia may benefit from receiving G-CSF in all subsequent cycles. If G-CSF is not used, the EUROTAX dose should be reduced from 75 to 60 mg/m^2. Patients who experience grade 3 or 4 stomatitis or oesophagitis should have their dose decreased to 60 mg/m^2 while the dose of other concomitant chemotherapy should also be reduced. EUROTAX should be stopped and not administered again in cases of grade 4 stomatitis or oesophagitis.

For capecitabine dose modifications when combined with EUROTAX, see capecitabine professional information.

For patients developing the first appearance of a grade 2 toxicity which persists at the time of the next EUROTAX/capecitabine treatment, delay treatment until resolved to grade 0-1, and resume at 100 % of the original dose. For patients developing the second appearance of a grade 2 toxicity, or the first appearance of a grade 3 toxicity, at any time during the treatment cycle, delay treatment until resolved to grade 0-1, then resume treatment with EUROTAX 55 mg/m^2. For any subsequent appearances of toxicities, or any grade 4 toxicities, discontinue the EUROTAX dose.

For EUROTAX dose modifications due to hepatic impairment, see section 4.4.

Combination therapy with EUROTAX for Gastric Cancer:

Patients treated with EUROTAX in combination with cisplatin and 5-fluorouracil must receive anti-emetics and appropriate hydration according to current institutional guidelines.

G-CSF should be administered to mitigate the risk of complicated neutropenia.

If an episode of febrile neutropenia, prolonged neutropenia or neutropenic infection occurs despite G-CSF use, the EUROTAX dose should be reduced from 75 to 60 mg/m^2.

If subsequent episodes of complicated neutropenia occur the EUROTAX dose should be reduced from 60 to 45 mg/m^2. In case of grade 4 thrombocytopenia the EUROTAX dose should be reduced from 75 to 60 mg/m^2. Patients should not be retreated with subsequent cycles of EUROTAX until neutrophils recover to a level > 1 500 cells/mm^3 and platelets recover to a level > 100 000 cells/mm^3. Discontinue treatment if these toxicities persist.

Recommended dose modifications for gastrointestinal toxicities in patients with EUROTAX in combination with cisplatin and 5-flurouracil (5-FU):

Toxicity	Dosage adjustment
Diarrhoea grade 3	First episode: reduce fluorouracil (5-FU) dose by 20 %. Second episode: then reduce EUROTAX dose by 20 %.
Diarrhoea grade 4	First episode: reduce EUROTAX and fluorouracil (5-FU) doses by 20 %. Second episode: discontinue treatment.
Stomatitis grade 3	First episode: reduce fluorouracil (5-FU) dose by 20 %. Second episode: stop fluorouracil (5-FU) only, at all subsequent cycles. Third episode: reduce EUROTAX dose by 20 %.
Stomatitis grade 4	First episode: stop fluorouracil (5-FU) only, at all subsequent cycles. Second episode: reduce EUROTAX dose by 20 %.

For cisplatin and 5-fluorouracil dosage adjustments, see local professional information leaflet.

Special populations

Patients with hepatic impairment:

Patients with bilirubin > ULN should generally not receive EUROTAX. Also, patients with AST and/or ALT > 1,5 x ULN concomitant with alkaline phosphatase > 2,5 x ULN, should generally not receive EUROTAX (see section 4.3).

Children:

The safety and effectiveness of EUROTAX in children have not been established (see section 4.3).

Elderly patients:

Based on a population pharmacokinetic analysis, there are no special instructions for the use in the elderly. For capecitabine dosage reduction when combined with EUROTAX, see capecitabine professional information.

Method of administration

EUROTAX should be administered by intravenous infusion only.

EUROTAX is administered as a one-hour infusion every three weeks.

For instruction on reconstitution of the medicinal product before administration, further handling and disposal, see section 6.6.

Directions for use:

Preparation for intravenous administration

Preparation of the infusion solution:

DO NOT use the two-vial formulation (injection concentrate and diluent) with the one-vial formulation.

If the vials are stored under refrigeration, allow the required number of EUROTAX cartons to stand at room temperature (below 25 °C) for 5 minutes before use.

More than one EUROTAX concentrate vial may be necessary to obtain the required dose for the patients. Based on the required dose for the patient expressed in mg, aseptically withdraw the required amount of EUROTAX concentrate solution using a calibrated syringe.

Inject the required concentrate volume into a 250 ml infusion bag or bottle containing either 50 mg/ ml (5 %) glucose solution or 9 mg/ ml (0,9 %) sodium chloride solution. If a dose greater than 200 mg of EUROTAX is required, use a larger volume of the infusion vehicle so that a concentration of 0,74 mg/ml docetaxel is not exceeded.

Mix the infusion bag or bottle manually using a rocking motion.

The EUROTAX infusion solution should be aseptically administered intravenously as soon as possible after preparation as a one-hour infusion, under room temperature and normal lighting conditions. The total duration of manipulation from start of the preparation of the bag to the end of the infusion must not exceed 4 hours.

EUROTAX infusion solution should be visually inspected prior to use.

Solutions containing a precipitate should be discarded.

Do not admix with other medicines.

EUROTAX infusion is compatible with commonly available administration sets, including PVC sets.

Any unused product or waste material should be disposed of in accordance with local requirements.

4.3 Contraindications

Hypersensitivity reactions to docetaxel or polysorbate 80 or any of the ingredients of EUROTAX (see section 6.1).

EUROTAX should not be used in patients with baseline neutrophil count of <1500 cells/mm^3.

EUROTAX is contraindicated during pregnancy and lactation as docetaxel is teratogenic in animals (see section 4.6).

The safe use of EUROTAX in children has not been established.

EUROTAX should not be used in patients with severe liver impairment since there is no data available (see section 4.4 and 4.2).

Contraindications for other medicines also apply when combined with EUROTAX.

4.4 Special warnings and precautions for use

Administration of EUROTAX (docetaxel) concentrate for solution for infusion should be done under the supervision of a medical practitioner/ oncologist experienced in the use of antineoplastic medicines. Appropriate management of complications is possible only when adequate diagnostic and treatment facilities are readily available.

EUROTAX therapy is associated with the incidence of treatment-related mortality which is increased in patients with abnormal liver function and in patients receiving higher doses. EUROTAX should generally not be given 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 transaminase concurrent with alkaline phosphatase are at increased risk for the development of grade 4 neutropenia, febrile neutropenia, infections, severe thrombocytopenia, severe stomatitis, severe skin toxicity and toxic death.

Patients with isolated elevations of transaminase > 1,5 x ULN also had a higher rate of febrile neutropenia grade 4 but did not have an increased incidence of toxic death.

Prior to each cycle of EUROTAX therapy, the treating doctor should review the values of Bilirubin, AST or ALT and alkaline phosphatase in the patient. Patients with neutrophil counts of < 1500 cells/mm^3 should not receive EUROTAX therapy. Frequent blood cell counts should be performed on all patients receiving EUROTAX therapy, in order to monitor

the occurrence of neutropenia (which may be severe and result in infections).

Studies have shown that severe hypersensitivity reactions that are characterised by hypotension and/or bronchospasm, or generalised rash/erythema occurred in 2,2 % of patients who received the recommended 3-day dexamethasone premedication. Hypersensitivity reactions requiring discontinuation of the EUROTAX infusion therapy were reported in some patients who did not receive the premedication. These reactions resolved after discontinuation of the infusion and the administration of appropriate therapy.

EUROTAX should not be given to patients who have a history of severe hypersensitivity to docetaxel or to any other ingredients in EUROTAX.

Studies have shown that severe fluid retention occurred in some patients despite the use of the recommended dexamethasone premedication. The fluid retention was characterised by one or more of the following events: severe peripheral oedema, generalised oedema, pleural effusion requiring urgent drainage, resting dyspnoea, cardiac tamponade or pronounced abdominal distention (due to ascites).

The use of EUROTAX infusion should be confined to departments specialised in the administration of cytotoxic chemotherapy and it should only be administered under the supervision of a qualified oncologist. Appropriate supportive equipment should be available, since significant hypersensitivity reactions may occur. Vital functions should be closely monitored during the infusion.

Premedication with a corticosteroid

It is recommended that premedication consisting of an oral corticosteroid such as Dexamethasone 16 mg per day (8 mg twice daily) for 3 days, is given to a patient due to receive EUROTAX infusion therapy. The premedication should start one day prior to EUROTAX administration, unless contraindicated. The premedication may reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions. For prostate cancer, the recommended pre-treatment regimen is oral dexamethasone 8 mg,

at 12 hours, 3 hours and 1 hour before the EUROTAX administration.

Neutropenia:

The most frequent reaction of EUROTAX is neutropenia and occurs in almost all patients. Studies have shown that severe neutropenia (grade 3-4) occurred in 99 % of patients on combination therapy with doxorubicin.

Studies show that neutrophil nadirs occurred at a median of 7-days, but this interval may be shorter in heavily pre-treated patients. Frequent monitoring of complete blood counts should be conducted on all patients receiving EUROTAX treatment. Patients should only be re-treated with EUROTAX after neutrophils recover to a level > 1500 cells/mm^3 (see section 4.2).

During a course of EUROTAX therapy, in the case of severe neutropenia (< 500 cells/mm^3 for 7-days or more), a dose reduction for subsequent courses of therapy and the use of appropriate symptomatic measures are recommended.

In patients treated with EUROTAX in combination with cisplatin and 5-flurouracil (TCF), febrile neutropenia and/or neutropenic infection occurred at lower rates when patients received prophylactic G-CSF. Patients treated with TCF should receive prophylactic G-CSF to mitigate the risk of complicated neutropenia (febrile neutropenia, prolonged neutropenia or neutropenic infection). Patients receiving TCF should be closely monitored.

Gastrointestinal reactions:

Caution is recommended for patients with neutropenia, particularly at risk for developing gastrointestinal complications. Enterocolitis could develop at any time, and could lead to death as early as on the first day of onset. Patients should be closely monitored for early manifestations of serious gastrointestinal toxicity (see above and section 4.8).

Hypersensitivity reactions:

Patients should be closely monitored for hypersensitivity reactions, especially during the first and second infusions with EUROTAX. Hypersensitivity reactions may occur within a few

minutes following the initiation of the infusion of EUROTAX. Facilities for the treatment of hypotension and bronchospasm should be readily available. If hypersensitivity reactions occur, minor symptoms such as flushing or localised cutaneous reactions do not require interruption of therapy.

More severe reactions, such as hypotension with a reduction of more than 20 mm Hg, bronchospasm or generalised rash/erythema, require immediate discontinuation of the infusion and appropriate symptomatic therapy.

Patients that have developed severe hypersensitivity reactions should not be re-treated with EUROTAX.

Patients who have previously experienced a hypersensitivity reaction to paclitaxel may develop a potentially fatal hypersensitivity reaction to EUROTAX.

Fluid retention:

Fluid retention, as well as other hypersensitivity reactions, may be reduced by administering a premedication consisting of oral dexamethasone 16 mg per day (8 mg twice per day) for 3-days, starting one day before treatment with EUROTAX.

Patients with severe fluid retention such as pleural effusion, pericardial effusion and ascites should be closely monitored when receiving treatment with EUROTAX.

Respiratory disorders:

Acute respiratory distress syndrome, interstitial pneumonia/pneumonitis, interstitial lung disease, pulmonary fibrosis and respiratory failure have been reported and may be associated with fatal outcome. Cases of radiation pneumonitis have been reported in patients receiving concomitant radiotherapy.

If new or worsening pulmonary symptoms develop, patients should be closely monitored, promptly investigated, and appropriately treated. Interruption of docetaxel therapy is recommended until diagnosis is available. Early use of supportive care measures may help

improve the condition. The benefit of resuming docetaxel treatment must be carefully evaluated.

Patients with liver impairment:

In patients with severe liver impairment treated with EUROTAX at 100 mg/m^2 (patients who have serum transaminase levels (ALT and/or AST) greater than 1,5 times the upper limit of the normal range (ULN) concurrent with serum alkaline phosphatase levels greater than 2,5 times ULN), there is a higher risk of developing severe adverse reactions such as toxic deaths, including sepsis and gastrointestinal haemorrhage which can be fatal, febrile neutropenia, infections, thrombocytopenia, stomatitis and asthenia. Therefore, the recommended dose of EUROTAX in patients with an elevated liver function tests is 75 mg/m^2 and liver function tests should be measured at baseline and before each cycle (see section 4.2).

In patients with serum bilirubin levels > ULN and/or ALT and AST > 3,5 times the ULN concurrent with serum alkaline phosphatase levels > 6 times the ULN, no dose-reduction can be recommended and EUROTAX should not be used unless strictly indicated.

The amount of ethanol in EUROTAX should be taken into account when given to patients with hepatic impairment (see section 6.1).

Patients with renal impairment:

There are no data available in patients with severely impaired renal function treated with docetaxel.

Cutaneous reactions:

Localised skin erythema of the extremities (palms of the hands and soles of the feet) with oedema followed by desquamation (hand-foot syndrome) have been observed in studies of patients receiving treatment with docetaxel. This type of toxicity can lead to the interruption or discontinuation of treatment.

Severe cutaneous adverse reactions (SCARs) such as Stevens-Johnson syndrome (SJS),

toxic epidermal necrolysis (TEN) and acute generalised exanthematous pustulosis (AGEP) have been reported in association with EUROTAX treatment. Patients should be informed about the signs and symptoms of serious skin manifestations and monitored closely. In case SCARs are observed, treatment discontinuation should be considered.

Nervous system disorders:

Severe peripheral neurotoxicity including paraesthesia, dysaesthesia and pain has been observed in patients receiving treatment with docetaxel, as contained in EUROTAX and requires a dosage reduction. If symptoms persist, treatment should be stopped.

Cardiac toxicity:

Ventricular dysrhythmia including ventricular tachycardia (sometimes fatal) has been reported in patients treated with docetaxel in combination regimens including doxorubicin, 5-fluorouracil and/ or cyclophosphamide (see section 4.8).

Baseline cardiac assessment is recommended.

Eye disorders:

Cystoid macular oedema (CMO) has been reported in patients treated with docetaxel. Patients with impaired vision should undergo a prompt and complete ophthalmologic examination. In case CMO is diagnosed, docetaxel treatment should be discontinued and appropriate treatment initiated (see section 4.8).

Second primary malignancies:

Second primary malignancies have been reported when EUROTAX was given in combination with anticancer treatments known to be associated with second primary malignancies. Second primary malignancies (including acute myeloid leukaemia, myelodysplastic syndrome, non-Hodgkin lymphoma and renal cancer) may occur several months or years after docetaxel-containing therapy. Patients should be monitored for second

primary malignancies (see section 4.8).

Tumour lysis syndrome:

Tumour lysis syndrome has been reported with EUROTAX (see section 4.8). Patients at risk of tumour lysis syndrome (i.e. with renal impairment, hyperuricaemia, bulky tumour) should be closely monitored in order to properly manage this syndrome. Correction of dehydration and treatment of high uric acid levels are recommended prior to initiation of treatment.

Interactions:

The concomitant use of EUROTAX with strong CYP3A4 inhibitors (e.g. ketoconazole, itraconazole, clarithromycin, indinavir, nelfinavir, ritonavir, saquinavir, telithromycin and voriconazole) should be avoided (see section 4.5).

Elderly:

Safety data analysis done in patients 60 years or older receiving treatment with docetaxel, as contained in EUROTAX, and capecitabine combination therapy showed 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 under the age of 60 years. Treatment in patients 60 years or older should be carefully monitored.

In patients treated with docetaxel, as contained in EUROTAX every three weeks the incidence of anaemia, infection, nail changes, anorexia and weight loss, occurred at rates ≥ 10 % higher in patients who were 65 years or older compared to younger patients.

The incidence of the following adverse events (all grades): lethargy, stomatitis, diarrhoea, febrile neutropenia/neutropenic infection, occurred at rates ≥ 10 % higher in patients who were 65 years or older compared to younger patients. Elderly patients treated with TCF should be closely monitored.

Others:

Contraceptive measures should be taken by both men and women during treatment and for a minimum of ~~three~~ 6 months after cessation of EUROTAX therapy (see section 4.6).

Additional cautions for use in adjuvant treatment of breast cancer

Complicated neutropenia:

For patients who experience complicated neutropenia (prolonged neutropenia, febrile neutropenia or infection), G-CSF and dose reduction should be considered (see section 4.2).

Gastrointestinal reactions:

Symptoms such as early abdominal pain and tenderness, fever, diarrhoea, with or without neutropenia, may be early manifestations of serious gastrointestinal toxicity and should be evaluated and treated promptly.

Congestive heart failure (CHF):

Patients should be monitored for symptoms of congestive heart failure during therapy and during the follow up period. In patients treated with the TAC regimen for node positive breast cancer, the risk of CHF has been shown to be higher during the first year after treatment (see section 4.8 and 5.1).

Leukaemia:

In the docetaxel, doxorubicin and cyclophosphamide (TAC) treated patients, the risk of delayed myelodysplasia or myeloid leukaemia requires haematological follow up.

Patients with 4+ nodes:

As the benefit observed in patient with 4+ nodes are not statistically significant on disease-free survival (DFS) and overall survival (OS), the positive benefit/risk ratio for TAC in patients with 4+ nodes is not fully demonstrated.

Excipients

EUROTAX 20 mg

This medicine contains 40 % w/v ethanol (alcohol). i.e. up to 400 mg per (1 ml) vial, equivalent to 10 ml of beer or 4 ml of wine.

Harmful for those suffering from alcoholism.
To be taken into account in pregnant or breastfeeding women, children and high-risk groups such as patients with liver disease, or epilepsy.

EUROTAX 80 mg

This medicine contains 40 % w/v ethanol (alcohol). i.e. up to 1600 mg per (4 ml) vial, equivalent to 40 ml of beer or 16 ml wine.

Harmful for those suffering from alcoholism.
To be taken into account in pregnant or breastfeeding women, children and high-risk groups such as patients with liver disease, or epilepsy.

EUROTAX 140 mg

This medicine contains 40 % w/v ethanol (alcohol). i.e. up to 2800 mg per (7 ml) vial, equivalent to 70 ml of beer or 28 ml wine.

Harmful for those suffering from alcoholism.
To be taken into account in pregnant or breastfeeding women, children and high-risk groups such as patients with liver disease, or epilepsy.

A dose of 100 mg/m^2 of this medicine administered to an adult weighing 70 kg would result in exposure to 52 mg/kg of ethanol which may cause a rise in blood alcohol concentration

(BAC) of about 8 mg/100 ml.

Evaluate the blood alcohol concentration (BAC) daily during the whole period of treatment.

Consideration should be given to possible effects on the central nervous system.

The amount of ethanol in EUROTAX may alter the effects of other medicines.

The amount of ethanol in EUROTAX may impair the ability to drive or use machines (see section 4.7).

4.5 Interaction with other medicines and other forms of interaction

There have been no formal clinical studies to evaluate the interactions of EUROTAX.

In vitro studies have shown that the metabolism of docetaxel may be modified by the concomitant 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 troleandomycin. Caution should be exercised when treating patients with these medicines as concomitant therapy, since there is a potential for a significant interaction.

In case of combination with CYP3A4 inhibitors, the occurrence of EUROTAX adverse reactions may increase as a result of reduced metabolism. If the concomitant use of a strong CYP3A4 inhibitor (e.g. ketoconazole, itraconazole, clarithromycin, indinavir, nelfinavir, ritonavir, saquinavir, telithromycin, troleandomycin and voriconazole) cannot be avoided, a close clinical surveillance is warranted and a dose-adjustment of EUROTAX may be suitable during the treatment with the strong CYP3A4 inhibitor (see section 4.4). In a pharmacokinetic study, the co-administration of docetaxel with the strong CYP3A4 inhibitor ketoconazole leads to a significant decrease in docetaxel clearance by 49 %.

Docetaxel is highly protein bound (> 95 %). Although the *in vivo* possible interactions of EUROTAX with concomitantly administered medicines have not been formally investigated, studies have shown that *in vitro* interactions with tightly protein-bound medicines such as erythromycin, diphenhydramine, propranolol, propafenone, phenytoin, salicylate,

sulfamethoxazole and sodium valproate did not affect the protein binding of docetaxel. In addition, dexamethasone did not affect protein binding of docetaxel. Digoxin binding is not influenced by docetaxel.

In doxorubicin/docetaxel combination therapy, the clearance of docetaxel was increased.

EUROTAX Concentrate for Solution for Infusion contains 400 mg ethanol per ml concentrate. The amount of alcohol in EUROTAX may alter the effects of other medicines.

4.6 Fertility, pregnancy and lactation

Pregnancy and breastfeeding

Docetaxel has been shown to be teratogenic in animals. Therefore, EUROTAX is contraindicated during pregnancy and lactation (see section 4.3).

Women of childbearing potential /Contraception in males and females

Female patients and female sexual partners of male patients receiving EUROTAX, should be advised to avoid becoming pregnant and to use highly effective contraception, until the end of relevant systemic exposure to the genotoxic compound including potential genotoxic metabolites plus an additional 6 months after exposure (i.e. five half-lives after the last dose, plus 6 months which covers the growth and maturation phase of folliculogenesis).

Fertility

In studies, docetaxel has genotoxic effects and may alter male fertility.

Male patients treated with EUROTAX should be advised to use highly effective contraception, until the end of relevant systemic exposure to the genotoxic compound including potential genotoxic metabolites plus an additional 3 months after exposure (i.e. five half-lives after the last dose, plus 60-75 days for sperm production plus 10-14 days for the transport to epididymis).

Therefore, men being treated with EUROTAX are advised not to father a child during and up to 6 months after treatment and to seek advice on conservation of sperm prior to treatment.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. The amount of ethanol in EUROTAX may impair the patient's ability to drive or use machines (see section 4.4 - Excipients). Therefore, patients should be warned of the potential impact of the side effects of the product on the ability to drive or use machines and be advised not to drive or use machines if they experience these side effects during treatment.

4.8 Undesirable effects

a. Summary of the safety profile

The adverse reactions considered to be possibly or probably related to the administration of docetaxel have been obtained in:

- patients who received 100 mg/m² and 75 mg/m² of docetaxel as a single medicine respectively.
- patients who received docetaxel in combination with doxorubicin.
- patients who received docetaxel in combination with cisplatin.
- patients who received docetaxel in combination with capecitabine.
- patients who received docetaxel in combination with prednisone or prednisolone (clinically important treatment related adverse events are presented).
- Patients who received docetaxel in combination with doxorubicin and cyclophosphamide (clinically important treatment related adverse events are presented).
- head and neck cancer patients who received docetaxel in combination with cisplatin and 5 fluorouracil (clinically important treatment related adverse events are presented).

The reactions are described according to the MedDRA system organ classification.

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Blood and lymphatic system disorders

In clinical trials with docetaxel, as contained in EUROTAX, the most frequently reported adverse reactions of docetaxel alone are: neutropenia (in patients who did not receive G-CSF, which is reversible and not cumulative; the median day to nadir is 7 days and the median duration of severe neutropenia (< 500 cells/mm^3) is 7 days), anaemia, alopecia, nausea, vomiting, stomatitis, diarrhoea and asthenia. The severity of adverse events of EUROTAX may be increased when it is given in combination with other chemotherapeutic medicines.

The following adverse reactions are frequently observed with docetaxel, as contained in EUROTAX:

Immune system disorders

Hypersensitivity reactions have generally occurred within a few minutes following the start of the infusion of docetaxel and are usually mild to moderate. The most frequently reported symptoms are flushing, rash with or without pruritus, chest tightness, back pain, dyspnoea and fever or chills. Severe anaphylactic reactions are characterised by hypotension and/or bronchospasm or generalized rash/erythema requiring therapeutic intervention may occur (see section 4.4). These may resolve after discontinuing the infusion and appropriate therapy.

Nervous system disorders

The development of severe peripheral neurotoxicity requires a reduction of dose (see sections 4.2 and 4.4). Mild to moderate neuro-sensory signs are characterised by paraesthesia, dysesthesia or pain including burning. Neuro-motor events are mainly characterised by weakness.

In some cases these events are reversible within 3 months in patients with neurotoxicity following the treatment of docetaxel, as in EUROTAX at 100 mg/m^2 as a single medicine.

Vascular disorders

Fluid retention includes events such as peripheral oedema and less frequently pleural effusion, pericardial effusion, ascites increased capillary permeability, and weight gain. The peripheral oedema usually starts at the lower extremities and may become generalised with a weight gain of 3 kg or more. Fluid retention is cumulative in incidence and severity (see section 4.4). Studies showed that the onset of moderate and severe retention is delayed in patients with premedication compared with patients without premedication, however, it has been reported in some patients during the early courses of therapy. The median time to fluid retention reversibility was 16,4 weeks (range 0 to 42 weeks) in patients receiving the recommended premedication.

Fluid retention has been less frequently reported in patients receiving the recommended premedication compared with patients without premedication.

Gastrointestinal disorders

Gastrointestinal effects such as nausea, vomiting, diarrhoea, abdominal pain and constipation may occur.

Stomatitis, oesophagitis and taste perversion may occur.

Gastrointestinal bleeding may occur.

Anorexia may occur and may be severe.

Hepato-biliary disorders

It has been observed that patients treated with docetaxel, as in EUROTAX at 100 mg/m^2 as a single medicine, increases the serum levels of AST, ALT, bilirubin and alkaline phosphatase greater than 2,5 times the ULN.

In patients treated at 75 mg/m^2 as a single medicine, no NCI grade 3 – 4 increased in serum levels of AST, ALT and alkaline phosphatase were observed and less than 2 % of the patients experienced grade 3 – 4 increase in bilirubin.

In patients treated in combination with doxorubicin at 75 mg/m^2, less than 1 % of patients experienced grade 3 – 4 increases in AST and ALT. Grade 3 – 4 increase in bilirubin and alkaline phosphatase were observed in less than 2,5 % of the patients.

Skin and subcutaneous tissue disorders

Reversible cutaneous reactions have been observed and are generally considered as mild to moderate. The majority of these events were reversible within 21 days. Reactions are characterised by a rash including localised eruptions mainly on the feet and hands (including severe hand and foot syndrome), but also on the arms, face or thorax, and frequently associated with pruritus. Eruptions generally occurred within one week after the docetaxel infusion. Less frequently, severe symptoms such as eruptions followed by desquamation which rarely led to interruption or discontinuation of docetaxel treatment were reported (see sections 4.2 and 4.4). Severe nail disorders are characterised by hypo- or hyperpigmentation and sometimes pain and onycholysis.

General disorders and administration site conditions

Infusion site reactions are generally mild and consisted of hyper pigmentation, inflammation, redness or dryness of the skin, phlebitis or extravasation and swelling of the vein.

Other

In patients treated with docetaxel, as in Eurotax 100 mg/m^2 as a single medicine, alopecia and asthenia has been observed in a majority of patients.

Arthralgias and myalgia may occur.

Dyspnoea may occur and is frequently associated with acute hypersensitivity reactions, respiratory infections and cancerous lung involvement.

Generalised or localised pain may occur, including chest pain without any cardiac or respiratory involvement.

b. Tabulated summary of adverse reactions

The following side effects to be considered in patients treated with EUROTAX:

MedDRA system organ classes	Frequent	Less frequent
Infections and infestations	Infection, including sepsis and pneumonia, fatal; Neutropenic infection; oral candidiasis	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Cancer pain	
Blood and lymphatic system disorders	Anaemia; Neutropenia; Thrombocytopenia; Febrile neutropenia	
Immune system disorders	Hypersensitivity	
Metabolism and nutrition disorders	Anorexia; Decreased appetite; Dehydration	
Nervous system disorders	Dysgeusia/ parosmia; Peripheral sensory neuropathy; Peripheral motor neuropathy; Paraesthesia; Dizziness; Headache	Syncope; Neurotoxicity; Somnolence
Eye disorders	Conjunctivitis; Lacrimation increased	
Ear and labyrinth disorders	Hearing impaired	
Cardiac disorders	Dysrhythmia; Cardiac failure; Myocardial ischemia	
Vascular disorders	Hot flush; Hypotension; Hypertension; Haemorrhage; Phlebitis; Venous disorder	Lymphoedema
Respiratory, thoracic and mediastinal disorders	Cough; Dyspnoea;	

	Pharyngolaryngeal pain; Epistaxis	
Gastrointestinal disorders	Nausea; Stomatitis/ Pharingitis; Vomiting; Diarrhoea; Constipation; Abdominal pain; Abdominal pain upper; Gastrointestinal haemorrhage; Dyspepsia, Dry mouth; Oesophagitis/ dysphagia/ odynophagia	
Skin and subcutaneous tissue disorders	Alopecia; Skin disorder/ reaction; Nail disorders (severe); Hand-foot syndrome; Dermatitis; Rash erythematous; Nail discolouration; Onycholysis; Exfoliative rash/ skin exfoliative Rash pruritic; Dry skin; Desquamation	
Musculoskeletal and connective tissue disorders	Myalgia (severe); Arthralgia; Pain in extremity; Back pain	
Reproductive system and breast disorders	Amenorrhoea	
General disorders and administration site conditions	Asthenia (severe); Pyrexia/ fever in absence of infection; Oedema/ Oedema peripheral/ fluid retention (severe); Pain; Infusion site reaction; Non-cardiac chest pain; Fatigue/ weakness;	

	Lethargy	
Investigations	Weight increased; Weight decreased; Blood bilirubin increased; Blood alkaline phosphatase increased; AST increased; ALT increased	

Post-marketing experience

Neoplasms benign, malignant and unspecified (including cysts and polyps)

Cases of acute myeloid leukaemia and myelodysplastic syndrome have been reported in association with docetaxel when used in combination with other chemotherapy medicines and/or radiotherapy.

Second primary malignancies, including non-Hodgkin lymphoma and renal cancer, have been reported in association with EUROTAX when used in combination with other anticancer treatments known to be associated with second primary malignancies.

Blood and lymphatic system disorders

Bone marrow suppression and other haematologic adverse reactions have been reported. Disseminated intravascular coagulation (DIC), often in association with sepsis or multi-organ failure, has been reported.

Immune system disorders

Some cases of anaphylactic shock, sometimes fatal, have been reported in patients who received premedication.

Hypersensitivity reactions (frequency unknown) have been reported with docetaxel in patients who previously experienced hypersensitivity reactions to paclitaxel.

Nervous system disorders

Less frequent cases of convulsion or transient loss of consciousness have been observed with docetaxel administration. These reactions sometimes appear during the infusion of the medicine.

Eye disorders

Less frequent cases of transient visual disturbances (flashes, flashing lights, scotomata) typically occurring during infusion of the medicinal product and in association with hypersensitivity reactions have been reported. These were reversible upon discontinuation of the infusion. Cases of lacrimation with or without conjunctivitis, as cases of lacrimal duct obstruction resulting in excessive tearing have been rarely reported. Cases of cystoid macular oedema (CMO) have been reported in patients treated with docetaxel.

Ear and labyrinth disorders

Less frequent cases of ototoxicity, hearing impairment and/or hearing loss have been reported, including cases associated with other ototoxic medicines.

Cardiac disorders

Less frequent cases of myocardial infarction have been reported.
Ventricular arrhythmia including ventricular tachycardia (frequency unknown), sometimes fatal, has been reported in patients treated with docetaxel in combination regimens including doxorubicin, 5-fluorouracil and/ or cyclophosphamide.

Vascular disorders

Venous thromboembolic events have less frequently been reported.

Respiratory, thoracic and mediastinal disorders

Acute respiratory distress syndrome, and cases of interstitial pneumonia / pneumonitis, interstitial lung disease, pulmonary fibrosis and respiratory failure sometimes fatal have less

frequently been reported, and may be associated with fatal outcome. Less frequent cases of radiation pneumonitis have been reported in patients receiving concomitant radiotherapy.

Gastrointestinal disorders

Less frequent occurrences of dehydration as a consequence of gastrointestinal events, gastrointestinal perforation, colitis ischaemic, colitis and neutropenic enterocolitis have been reported with a potential fatal outcome. Less frequent cases of ileus and intestinal obstruction have been reported.

Hepatobiliary disorders

Less frequent cases of hepatitis, sometimes fatal primarily in patients with pre-existing liver disorders, have been reported.

Skin and subcutaneous tissue disorders

Less frequent cases of cutaneous lupus erythematosus and bullous eruptions such as erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis and acute generalised exanthematous pustulosis, have been reported with docetaxel, as in EUROTAX. In some cases, concomitant factors may have contributed to the development of these effects. Sclerodermal-like changes usually preceded by peripheral lymphoedema have been reported with docetaxel. Cases of permanent alopecia (frequency unknown) have been reported.

Renal and urinary disorders

Renal insufficiency and renal failure have been reported. In about 20% of these cases there were no risk factors for acute renal failure such as concomitant nephrotoxic medicines and gastrointestinal disorders.

General disorders and administration site conditions

Radiation recall phenomena have less frequently been reported, and may be associated with fatal outcome.

Injection site recall reaction (recurrence of skin reaction at a site of previous extravasation following administration of docetaxel at a different site) has been observed at the site of previous extravasation (frequency unknown).

Fluid retention has not been accompanied by acute episodes of oliguria or hypotension.

Dehydration and pulmonary oedema have less frequently been reported.

Metabolism and nutrition disorders

Cases of electrolyte imbalance have been reported. Cases of hyponatraemia have been reported, mostly associated with dehydration, vomiting and pneumonia.

Hypokalaemia, hypomagnesaemia, and hypocalcaemia were observed, usually in association with gastrointestinal disorders and in particular with diarrhoea. Tumour lysis syndrome, sometimes fatal, has been reported.

Musculoskeletal disorders

Myositis has been reported with EUROTAX.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website or to Eurolab (Pty) Ltd. by email: drug-safety@eurolab.co.za. By reporting side effects, you can help provide more information on the safety of EUROTAX.

4.9 Overdose

In case of overdose with EUROTAX, the patient should be kept in a specialised medical unit and vital functions should be closely monitored. There is no known antidote for EUROTAX overdosage. The primary anticipated complications of overdosage consist of neutropenia, mucositis, cutaneous reactions and paraesthesia.

Patients should receive therapeutic G-CSF as soon as possible after discovery of overdose. Other appropriate symptomatic treatment measures should be taken, as needed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antineoplastic agents, Taxanes, ATC Code: LO1CD02

A26 Cytostatic agents

Mechanism of action

Docetaxel is an antineoplastic medicine which acts by promoting the assembly of tubulin into stable microtubules and inhibits their disassembly which leads to a marked decrease of free tubulin. The binding of docetaxel to microtubules does not alter the number of protofilaments. Docetaxel has been shown *in vitro* to disrupt the microtubular network in cells which is essential for vital mitotic and interphase cellular functions.

Pharmacodynamic effects

Docetaxel was found to be cytotoxic *in vitro* against various murine and human tumour cell lines and against freshly excised human tumour cells in clonogenic assays. Docetaxel achieves high intracellular concentrations with a long cell residence time. In addition, docetaxel was found to be active on some but not all cell lines overexpressing the p-glycoprotein which is encoded by the multidrug resistance gene.

5.2 Pharmacokinetic properties

Absorption

The pharmacokinetics of docetaxel have been evaluated in cancer patients after administration of 20 - 115 mg/m^2 in Phase I studies. The kinetic profile of docetaxel is dose

independent and consistent with a three-compartment pharmacokinetic model with half-lives for the alpha, beta and gamma phases of 4 minutes, 36 minutes and 11,1 hours respectively. The late phase is due, in part, to a relatively slow efflux of docetaxel from the peripheral compartment.

Distribution

Following the administration of a 100 mg/m^2 dose given as a one-hour infusion, a mean peak plasma level of 3,7 µg/ml was obtained with a corresponding AUC of 4,6 h.µg/ml. Mean values for total body clearance and steady state volume of distribution were 21 l/h/m^2 and 113 l, respectively.

Docetaxel is more than 95 % bound to plasma proteins.

Biotransformation

Based on *in vitro* studies, isoenzymes of the cytochrome P450-3A subfamily appear to be involved in docetaxel metabolism. Dexamethasone did not affect protein binding of docetaxel.

Elimination

Faecal excretion is the main route of elimination of docetaxel and its metabolites. The faecal and urinary excretions account for about 75 % and 6 % of the dose, respectively. Only a minor fraction of the dose is excreted as the parent compound.

<u>Combination therapy</u>

Doxorubicin

When used in combination, docetaxel does not influence the clearance of doxorubicin and the plasma levels of doxorubicinol (a doxorubicin metabolite). However, the clearance of docetaxel was increased. The pharmacokinetics of docetaxel, doxorubicin and cyclophosphamide were not influenced by their coadministration.

Cisplatin

Clearance of docetaxel in combination therapy with cisplatin was similar to that observed

following monotherapy. The pharmacokinetic profile of cisplatin administered shortly after docetaxel infusion is similar to that observed with cisplatin alone.

Capecitabine

Phase I study evaluating the effect of capecitabine on the pharmacokinetics of docetaxel and vice versa showed no effect by capecitabine on the pharmacokinetics of docetaxel (C_{max} and AUC) and no effect by docetaxel on the pharmacokinetics of a relevant capecitabine metabolite 5'-DFUR.

Prednisone and dexamethasone

The effect of prednisone on the pharmacokinetics of docetaxel administered with standard dexamethasone premedication has been studied in 42 patients. No effect of prednisone on the pharmacokinetics of docetaxel was observed.

5.3 Preclinical safety data

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid anhydrous

Povidone

Polysorbate 80

Ethanol absolute

6.2 Incompatibilities

EUROTAX must not be mixed with other medicinal products except those mentioned in 6.6.

6.3 Shelf life

Unopened vial:

24 months.

After opening of the vial:

Each vial is for single use and should be used immediately after opening. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Once added to the infusion bag:

From a microbiological point of view, reconstitution/dilution must take place in controlled and aseptic conditions and the medicinal product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Once added as recommended into the infusion bag, the docetaxel infusion solution, if stored below 25°C, in non-PVC bags, is stable for 8 hours. It should be used within 8 hours (including the one-hour infusion intravenous administration).

In addition, physical and chemical in-use stability of the infusion solution prepared as recommended has been demonstrated for 3 days when stored between 2 to 8°C protected from light. EUROTAX infusion solution is supersaturated, therefore may crystallize over time. If crystals appear, the solution must no longer be used and shall be discarded.

6.4 Special precautions for storage

Store at or below 25 °C, in the original packaging, protected from light. Do not refrigerate or freeze.

For storage conditions after opening of the vials and of the diluted medicinal product, see section 6.3.

6.5 Nature and contents of container

EUROTAX 20 mg/1 ml: One 5 ml colourless glass vial with a grey rubber stopper and an aluminium flip off cap.

The vial can be with or without overwrapping/sleeving, included or not in a thermoformed tray, packed in a carton box.

EUROTAX 80 mg/4 ml: One 8 ml or 10 ml colourless glass vial with a grey rubber stopper and an aluminium flip off cap.

The vial can be with or without overwrapping/sleeving, included or not in a thermoformed tray, packed in a carton box.

EUROTAX 140 mg/7 ml: One 11 ml or 10 ml colourless glass vial with a grey rubber stopper and an aluminium flip off cap.

The vial can be with or without overwrapping/sleeving, included or not in a thermoformed tray, packed in a carton box.

6.6 Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product

Recommendations for safe handling:

Handling precautions for cytostatic medicines should be followed:

- Only trained personnel should reconstitute the medicine in a designated area.
- EUROTAX is an antineoplastic medicine and, as with other potentially toxic compounds, caution should be exercised when handling it and preparing EUROTAX solutions.
- The work surface should be covered with disposable plastic-backed absorbent paper.
- Adequate protective gloves and clothing should be worn.
- If EUROTAX concentrate or infusion solution should come into contact with the skin, wash immediately and thoroughly with soap and water. If EUROTAX concentrate or infusion solution should come into contact with the eyes or mucous membranes, wash immediately and thoroughly with water.
- The cytotoxic preparation must not be handled by pregnant staff.
- Adequate care and precautions should be taken in the disposal of items used to reconstitute the medicine.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Eurolab (Pty) Ltd.

Woodmead Office Park, 3 Stirrup Lane

Van Reenens Avenue

Woodmead, 2144

8 REGISTRATION NUMBER(S)

EUROTAX 20: 52/26/0263

EUROTAX 80: 52/26/0264

EUROTAX 140: 52/26/0265

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

02 June 2020

10 DATE OF REVISION OF THE TEXT

27 June 2025