Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Mitoxantrone 2mg/ml Concentrate for solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 2mg of Mitoxantrone (as hydrochloride).

Each 10ml vial contains 20mg of Mitoxantrone (as hydrochloride)

This medicinal product contains 1.38mmole sodium and 1mg of sodium metabisulfite per 10ml vial.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Concentrate for Solution for Infusion.

A dark-blue solution with pH 3.0 – 4.5 and osmolarity 240 to 360 mOsmol/kg

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Mitoxantrone is indicated in the treatment of metastatic breast cancer, non-Hodgkin's lymphoma and adult acute non-lymphocytic leukaemia.

4.2 Posology and method of administration

FOR INTRAVENEOUS USE ONLY.

Mitoxantrone should be given by intravenous infusion.
Mitoxantrone concentrate must be diluted prior to use.
Care should be taken to avoid contact of mitoxantrone with skin, mucous membranes or eyes. See section 6.6 Instructions for use and handling for further directions.

For single use only. Any unused solution should be discarded.

Syringes containing this product should be labeled ‘MITOXANTRONE, FOR INTRAVENOUS USE ONLY’.

Metastatic breast cancer, Non-Hodgkin's lymphoma:

a) Single Agent Dosage:

The recommended initial dosage of Mitoxantrone as a single agent is 14 mg/m2 of body surface area, given as a single intravenousdose which may be repeated at 21-day intervals. A lower initial dosage (12 mg/m2 or less) is recommended in patients with inadequate bone marrowreserves e.g. due to prior chemotherapy or poor general condition.

Dosage modification and the timing of subsequent dosing should be determined by clinical judgment depending on the degree and duration ofmyelosuppression. For subsequent courses the prior dose can usually be repeated if white blood cell and platelet counts have returned to normal levels after21 days. The following table is suggested as a guide to dosage adjustment in the treatment of metastatic breast cancer andnon-Hodgkin's lymphoma according to haematological nadir (which usually occurs about 10 days after dosing).

Nadir after prior dose:

WBC (per mm^3)	**Platelets (per mm^3)**	**Time to recovery**	**Subsequent dose after adequate haematological recovery**
>1,500 AND	>50,000	21 days	Repeat prior dose after recovery
>1,500 AND	>50,000	>21 days	Withhold until recovery then repeat prior dose
<1,500 OR	<50,000	Any duration	Decrease by 2mg/m^2 from prior dose after recovery
<1,000 OR	<25,000	Any duration	Decrease by 4mg/m^2 from prior dose after recovery

b) Combination Therapy:

Mitoxantrone has been administered as a component of a combination therapy. In cases of metastatic breast cancer, combinations of mitoxantrone with othercytotoxic agents including cyclophosphamide and 5-fluorouracil, or methotrexate and mitomycin C, appeared to be effective. For information on dose adjustments and method of administration, please refer to the published literature.

As a guide, when mitoxantrone is used in combination chemotherapy with another myelosuppressive agent, the initial dose of mitoxantrone should bereduced by 2-4 mg/m2 below the doses recommended for single agent use. Subsequent doses, as outlined in the table above, depend on the degree andduration of myelosuppression.

Adult acute non-lymphocytic leukaemia:

(a) Single Agent Dosage in Relapse:

The recommended dosage for remission induction is 12 mg/m2 of body surface area, given as a single intravenous dosedaily for five consecutive days (total of 60 mg/m2). In clinical studies with a dosage of 12 mg/m2 daily for 5 days, patients who achieved a completeremission did so as a result of the first induction course.

(b) Combination Therapy:

Mitoxantrone has been used in combination regimens for the treatment of acute non-lymphocytic leukaemia (ANLL). Most clinicalexperience has been with Mitoxantrone combined with cytosine arabinoside. This combination has been used successfully for primary treatment of ANLL as well as inthe treatment of relapse.

Use cytarabine between parentheses following the “cytosine arabinoside”.

An effective regimen for induction in previously untreated patients has been Mitoxantrone 10-12 mg/m2 IV for 3 days combined with cytosine arabinoside 100 mg/m2IV for 7 days (by continuous infusion). This is followed by second induction and consolidation courses as thought appropriate by the treating clinician. Inclinical studies, duration of therapy in induction and consolidation courses with mitoxantrone have been reduced to 2 days, and that of cytosine arabinosideto 5 days.However, modification to the above regimen should be carried out by the treating clinician depending on individual patient factors.

Efficacy has also been demonstrated with Mitoxantrone in combination with etoposide in patients who had relapsed or who were refractory to primaryconventional chemotherapy. The use of Mitoxantrone in combination with etoposide, as with other cytotoxics, may result in greater myelosuppression thanwith Mitoxantrone alone.

Reference should be made to the published literature for information on specific dosage regimens. Mitoxantrone should be used by clinicians experienced inthe use of chemotherapy regimens. Dosage adjustments should be made by the treating clinician as appropriate, taking into account toxicity, response and individual patient characteristics.

(c) Children and adolescents:

As experience with Mitoxantrone in paediatric leukaemia is limited, dosage recommendations in this patient population cannot at present be given.

Hepatic impairment
Mitoxantrone is not recommended in patients with abnormal liver function tests because its clearance is reduced by hepatic impairment and laboratory measurements cannot predict the degree of this. Therefore, appropriate dose adjustments cannot be recommended. Liver function tests should be performed prior to each course of therapy. Careful supervision is recommended when treating patients with severe hepatic insufficiency. The safety of Mitoxantrone in such patients has not been established.

Method of administration:
For intravenous use only.

Dilute the required volume of Mitoxantrone Sterile Concentrate to at least 50 ml in either of the following infusion solutions: sodium chloride 900mg/100ml glucose 5000mg/100ml, or sodium chloride 180mg/100ml and glucose 4000mg/100ml. Use Leur-lock fittings on all syringes and sets. Large bore needles are recommended to minimise pressure and the possible formation of aerosols.

The latter may also be reduced by the use of a venting needle.

Administer the resulting solution over not less than 3 minutes via the tubing of a freely running intravenous infusion of the above fluids. Mitoxantrone should not be mixed with other drugs in the same infusion.

If extravasation occurs, the administration should be stopped immediately and restarted in another vein.

4.3 Contraindications

- Not for subcutaneous, intramuscular, intrathecal or intra-arterial use. Severe injury with permanent sequelae can result from intrathecal administration. (See Section 4.4 Special Warnings and Precautions.)
- Use in patients with profound myelosuppression.
- Lactation (for pregnancy please refer to section 4.6 Pregnancy and lactation).
- Hypersensitivity to mitoxantrone or to any of the excipients.

4.4 Special warnings and precautions for use

Mitoxantrone is an active cytotoxic drug which should be used by clinicians familiar with the use of antineoplastic agents, and having the facilities for regular monitoring of clinical, haematological and biochemical parameters, as well as frequent patient observation, during and after treatment. This includes adjunctive therapies, including antibiotics.

Mitoxantrone should be given slowly into a freely flowing intravenous infusion.

Myelosuppression may be more severe and prolonged in patients with poor general condition, or prior chemotherapy and/or radiotherapy.

Increased risk of leukaemia and other malignancies:
There may be an increased risk of leukaemia when Mitoxantrone is used as adjuvant treatment of non-metastatic breast cancer. In the absence of sufficientefficacy data, Mitoxantrone must not be used as adjuvant treatment of non-metastatic breast cancer.
Mitoxantrone should be used with caution in patients with myelosuppression or poor general condition.

Mitoxantrone is mutagenic in vitro and in vivo in the rat. In the same species there was a possible association between administration of the drug and development of malignant neoplasia.

Topoisomerase II inhibitors, including Mitoxantrone hydrochloride, when used concomitantly with other antineoplastic agents and/or radiotherapy, have been associated with the development of Acute Myeloid Leukaemia (AML) or Myelodysplastic Syndrome (MDS).

Cardiac changes and monitoring:
Cases of functional cardiac changes, including congestive heart failure and decreases in left ventricular ejection fraction have been reported. The majority of these cardiac events have occurred in patients who have had prior treatment withanthracyclines, prior mediastinal/thoracic radiotherapy, or with pre-existing heart disease. It is recommended that patients in these categories are treated with mitoxantrone at full cytotoxicdosage and schedule. However, added caution is required in these patients and careful regular cardiac examinations are recommended from the initiation oftreatment.

As experience of prolonged treatment with Mitoxantrone is presently limited, it is suggested that cardiac monitoring should also be performed in patients without identifiable risk factors during therapy exceeding 160 mg/m2.

Hepatic Insufficiency:
Careful supervision is recommended when treating patients with hepatic insufficiency.

Allergic reactions:
Sulfites may rarely cause severe hypersensitivity reactions and bronchospasm.

Neurotoxicity and tissue damage/ extravasation:
Mitoxantrone is not indicated for intra-arterial injection. There have been reports of neuropathyand neurotoxicity, both central and peripheral, following intra-arterial injection. These reports have included seizures leading to coma and severe neurologic sequelae, and paralysis with bowel and bladder dysfunction.

Great care should be taken during administration to avoid extravasationat the infusion site as severe local tissue damage (requiring debridement and skin grafting) may result (See Section 4.4 Special Warnings and Precautions and Section 4.8 Undesirable Effects) and to avoid contact of Mitoxantrone with the skin, mucous membranes, or eyes. Signs or symptoms of extravasation include burning, pain, pruritus, erythema, swelling, blue discoloration, or ulceration however, it may occur without accompanying symptoms and even if blood has returned well on aspiration of the infusion needle.

If it is known or suspected that subcutaneous extravasation has occurred, the injection or infusion should be immediately stopped and restarted in another vein above the previous vein or in the contralateral arm. It is recommended that intermittent ice packs be placed over the area of extravasation and that the affected extremity be elevated. The ice pack should be applied for at least one hour, longer if pain persists. Because of the progressive nature of extravasation reactions, the area of injection should be frequently examined and surgery consultation obtained early if there is any sign of a local reaction. The extravasation site should be carefully monitored for signs of necrosis and/or phlebitis that may require further medical attention.

It must never be given subcutaneously, intramuscularly, or intra-arterially and extravasation results in severe local tissue damage. There have been reports of local/regional neuropathy, some irreversible, following intra-arterial injection.

Precautions for Use:
Mitoxantrone is an active cytotoxic drug which should be used by clinicians familiar with the use of antineoplastic agents and have the facilities forregular monitoring of clinical, haematological and biochemical parameters during and after treatment.
Full blood counts should be undertaken serially during a course of treatment. Dosage adjustments may be necessary based on these counts.

This medicinal product contains 1.38 mmol sodium per vial. To be taken into consideration by patients on a controlled sodium diet

Vaccination and Immunisation:
Immunization may be ineffective when given during Mitoxantrone therapy. Immunisation with live virus vaccines is

generally not recommended.

Discoloration of urine and other tissues:
Mitoxantrone may impart a blue-green coloration to the urine for 24 hours after administration, and patients should be advised to expect this during therapy. Blue discoloration of skin and nails has been reported occasionally and reversible blue coloration of the sclera may be seen very rarely.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use of Mitoxantrone with other antineoplastic agents and/or radiotherapy has been associated with the development of Acute Myeloid Leukaemia (AML) or Myelodysplastic Syndrome (MDS). (See also section 4.4 Special Warnings and Precautions for Use).

Mitoxantrone in combination with other myelosuppresive medicinal products may increase the myelotoxicity of mitoxantrone and/or that of the concomitant medicinal products."

Combination of mitoxantrone with potentially cardiotoxic medicinal products (e.g. other anthracyclines) increases the cardiac toxicity.

Immunisation may be ineffective when given during mitoxantrone therapy (immunisation with live virus vaccines should be avoided).

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6

4.6 Fertility, pregnancy and lactation

There are no adequate and well-controlled studies in pregnant women. Mitoxantrone should not normally be administered to patients who are pregnant. If the drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be advised of the potential hazard to the foetus. Women of childbearing potential and their partners should be advised to avoid becoming pregnant and use effective contraception during therapy and for at least six months after cessation of therapy.

Mitoxantrone is excreted in human milk and significant concentrations (18ng/ml) have been reported for 28 days after the last administration. Because ofthe potential for serious adverse reactions in infants from mitoxantrone, breast-feeding should be discontinued before starting treatment.

Mitoxantrone may be genotoxic. Men treated with Mitoxantrone are therefore recommended not to procreate a child during treatment and upto 6 months afterwards and to seek counseling about spermatic preservation prior to therapy due to the possibility of irreversible infertility as a result of therapy with Mitoxantrone.

4.7 Effects on ability to drive and use machines

Drowsiness and confusion have been reported. Patients should be advised not to drive, operate machinery or take part in activities where these symptoms could put themselves or others at risk.

4.8 Undesirable effects

Frequencies are defined using the following convention:
Very common (≥1/10);
common (≥1/100 to <1/10);
uncommon (≥1/1,000 to <1/100);
rare (≥1/10,000 to ≤1/1,000);
very rare (≤1/10,000),
not known (cannot be estimated from the available data).

More than 10 % of patients may have undesirable effects.

Myelosuppression is a dose limiting adverse reaction of mitoxantrone.
Myelosuppression may be more profound and prolonged in patients who previously have received chemotherapy or radiation therapy.

In case of hormone-resistant prostatic carcinoma:
In a randomized phase III study in which the mitoxantrone dose was increased as from a neutrophilic number > 1,000/mm^3, neutropenia of WHO grade 4 (ANC < 500/mm^3) was observed in 54% of patients receiving mitoxantrone and low-dosed prednisone. The median dose was 12 mg/m2; 36 in 84 patients received more than 12 mg/m^2 Mitoxantrone. In a separate randomised study in which patients were treated with 14 mg/m^2 mitoxantrone, neutropenia of grade 4 was observed in 23% of patients receiving mitoxantrone and hydrocortisone. Neutropenic fever and infections occurred in both studies in patients treated with mitoxantrone and hydrocortisone. The incidence of infections was 17% in one of the studies, and that of fever without infection was 14%; in the other study, systemic infections occurred in 10%, urinary tract infections in 9%, skin infections in 5% and fever in 6% of cases. In these studies, platelet counts < 50,000/mm^3 were observed in 4% and 3% of patients receiving mitoxantrone and corticosteroids.

Infections and infestations:
Very common: Infections.
Common: Upper respiratory tract infection, pneumonia, sepsis.
Frequency unknown: Urinary tract infection.

Neoplasms benign, malignant and unspecified (incl cysts and polyps):
Frequency unknown: Acute leukaemia.

Topoisomerase II inhibitors, including mitoxantrone, in combination with other antineoplastic agents and/or radiotherapy, have been associated with the development of acute myeloid leukaemia (AML) or myelodysplastic syndrome (MDS) (see also section 4.5. Interactions with other medicinal products and other forms of interaction).

Blood and the lymphatic system disorders:
Very common: Myelosuppression, bone marrow hypoplasia, leukopenia, granulocytopenia, neutropenia, thrombocytopenia, anaemia, abnormal amount of leucocytes.

Immune system disorders:
Uncommon: Immunosuppression, anaphylactic/anaphylactoide reaction (including anaphylactic shock), allergic reactions (including exanthema, dyspnoea, hypotension).

Metabolism and nutrition disorders:
Common: Anorexia
Frequency unknown: Hyperuricaemia

Psychiatric disorders:
Uncommon: Anxiety, confusion

Nervous system disorders:
Uncommon: Non-specific neurological undesirable effects such as dizziness, somnolence, neuritis, convulsion, paresthesia.
Headache.

Eye disorders:
Uncommon: Reversible blue coloration of the sclera, conjunctivitis.

Cardiac disorders:
Very common: Transient ECG changes after long-term treatment..
Common: Asymptomatic reduced left ventricular ejection fraction, cardiac insufficiency, chest pain,

congestive heart failure after long-term treatment (2.6% with a cumulative dose of 140 mg/m²).
Sinus bradycardia.
Uncommon: Acute arrhythmia.
Rare: Cardiomyopathy
Frequency unknown: Myocardial infarction.

The cardiac function should be monitored in patients who received cumulative doses >160 mg/m2 mitoxantrone.

Patients who previously have received anthracyclin or other cardiotoxic oncolytics and/or mediastinal radiation therapy and who also suffers from underlying cardiovascular disease, have a higher risk of cardiac affection.
Post-marketing reports have shown cardiotoxicity in treatment with mitoxantrone at cumulative doses of less than 100 mg/m^2.

Vascular disorders:
Very common: Haemorrhagia
Common: Hypotension

Respiratory, thoracic and mediastinal disorders:
Frequency unknown: Dyspnoea.

Gastrointestinal disorders:
Very common: Nausea and vomiting (in app. 50% of the patients, severe in 1%).
Mucositis, stomatitis, diarrhoea, constipation, loss of appetite, abdominal pain.
Common: Gastrointestinal bleeding.

Hepato-biliary disorders:
Common: Hepatotoxicity.
Uncommon: Transient increase of liver enzymes and bilirubin, severe impairment of hepatic function.

Skin and subcutaneous tissue disorders:
Very common: Alopecia grade I-II in app. 50% of the patients (severe alopecia is rare).
Common: Rash, erythema.
Uncommon: Blue discoloration of the skin and nails.
Frequency unknown: Nail disorders (eg onycholysis, nail dystrophy).
Extravasation at the infusion site which may result in erythema, swelling, pain, burning and/ or blue discoloration of the skin. Extravasation can result in tissue necrosis with resultant need for debridement and skin grafting.

Renal and urinary disorders:
Common: Nephrotoxicity.
Uncommon: Elevated serum creatinine and blood urea nitrogen levels.
Blue-green discolouration of the urine for 24 hours after administration.
Rare: Hyperuricaemia.

Reproductive System and breast disorders:
Uncommon: Amenorrhoea.

General disorders and administration site conditions:
Very common: Fever.
Common: Fatigue, oedema.
Frequency unknown: Phlebitis has also been reported at the site of infusion.
Weakness

Investigations:
Very rare: Change in weight.

Tumour lysis syndrome (characterised by hyperuricaemia, hyperkalaemia, hyperphosphataemia and hypocalcaemia) has been observed rarely during single-agent chemotherapy with mitoxantrone, as well as during combination chemotherapy.

In patients with leukaemia, the pattern of undesirable effects is generally similar, although there is an increase in both frequency and severity, particular of stomatitis and mucositis.

Two incidences of sudden death have been reported among patients with disseminated sclerosis treated with mitoxantrone. It is unknown whether there is a causal relationship with the use of mitoxantrone.

4.9 Overdose

There is no known specific antidote for Mitoxantrone. Haemopoietic, gastrointestinal, hepatic or renal toxicity may be seen, depending onthe dosage given and the physical condition of the patient. In cases of overdosage patients should be monitored closely and management should besymptomatic and supportive.

Fatalities have occurred on rare occasions as a result of severe leucopenia with infection in patients accidentally given single bolus injections of Mitoxantrone at over ten times the recommended dosage. Mitoxantrone is extensively tissue-bound and peritoneal dialysis or haemodialysis is unlikelyto be effective in managing overdose.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: L01D B07
Pharmacotherapeutic group: Anthracyclines and related substances.

Although its mechanism of action has not been determined, Mitoxantrone is a DNA-reactive agent. It has a cytocidal effect on proliferating and nonproliferatingcultured human cells, suggesting activity against rapidly proliferating and slow-growing neoplasms.

5.2 Pharmacokinetic properties

Animal pharmacokinetic studies in rats, dogs and monkeys given radiolabelledMitoxantrone indicate rapid, extensive dose proportional distribution into mosttissues.
Mitoxantrone does not cross the blood-brain barrier to any appreciable extent. Distribution into testes is relatively low. In pregnant rats the placenta is aneffective barrier.Plasma concentrations decrease rapidly during the first two hours and slowly thereafter. Animal data established biliary excretion as the major route ofelimination. In rats, tissue elimination half-life of radioactivity ranged from 20 days to 25 days as compared with plasma half-life of 12 days. Mitoxantrone isnot absorbed significantly in animals following oral administration.

Pharmacokinetic studies in patients following intravenous administration of Mitoxantrone demonstrated a triphasic plasma clearance. Distribution to tissues israpid and extensive. Elimination of the drug is slow with a mean half-life of 12 days (range 5-18) and persistent tissue concentrations. Similar estimates ofhalf-life were obtained from patients receiving a single dose of Mitoxantrone every 21 days and patients dosed on 5 consecutive days every 21 days.

Mitoxantrone is excreted via the renal and hepatobiliary systems. Only 20-32% of the administered dose was excreted within the first five days after dosing(urine 6-11%, faeces 13-25%). Of the material recovered in the urine 65% was unchanged Mitoxantrone and the remaining 35% is primarily comprised oftwo inactive metabolites and their glucuronide conjugates. Approximately two thirds of the excretion occurred during the first day.

5.3 Preclinical safety data

Reproductive toxicity:
Intravenous administration of mitoxantrone at doses which is 0.05 times the human dose (in mg/m2) to pregnant rats

resulted in low fetal birth weight and delayed renal development. In rabbits mitoxantrone caused premature births at doses which are 0.01 times the human dose. Mitoxantrone has no adverse effect on fertility in male and female rats.

Mutagenicity:
Mitoxantrone was mutagenic in in-vitro test systems with bacterial and mammalian species. Mitoxantrone showed an clastogenic effect in vitro in the liver cells of rats and in Chinese hamster ovary cells and in vivo on the bone marrow of rats.

Carcinogenesis: Mitoxantrone administered intravenously to rats and mice at intervals of 21 days resulted in an increased risk of fibroids and tumors of the outer auditory meatus in rats and hepatocellular adenomas in male mice at doses of 0.02 -0.03 times a humandose (mg/m2).

Animal data are too limited to draw conclusions regarding teratogenicity.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Glacial acetic acid
Sodium acetate anhydrous
Sodium metabisulfite (E223)
Water for Injections

6.2 Incompatibilities

Mitoxantrone must not be mixed in the same infusion as heparin since a precipitate may form.
In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

18 Months

Chemical and physical in use stability of the diluted product has been demonstrated for 24 hours at 25°C and for 72 hours at 2-8°C in:

- Sodium chloride 9 mg/ml (0.9 %),
- Glucose 50 mg/ml (5 %), or
- Sodium chloride 9 mg/ml (0.9 %) and Glucose 50 mg/ml (5 %) solution.

From a microbiological point of view, the diluted product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C.

6.4 Special precautions for storage

Store below 25°C. Do not refrigerate or freeze.

For storage conditions of the diluted medicinal product, see Section 6.3.

6.5 Nature and contents of container

20mm flint type I tubular glass vial filled to 10 ml. Each vial is sealed with a 20mm grey bromobutyl rubber stopper and 20mm violet flip off aluminum seal. Mitoxantrone is presented in packs of 1 vial.

6.6 Special precautions for disposal and other handling

a) Instructions for use

Mitoxantrone should be given by intravenous infusion.

For single use only.
Syringes containing this product should be labelled ‘FOR INTRAVENOUS USE ONLY’.

Care should be taken to avoid contact of mitoxantrone with skin, mucous membranes or eyes. Vials should be dispensed in upright position in order to prevent drops of Mitoxantrone collecting in the stopper during preparation and leading to potential aerosolisation of the solution.

Dilute the required volume of Mitoxantrone Injection to at least 50 ml using a solution of

- Sodium chloride 9 mg/ml (0.9 %),
- Glucose 50 mg/ml (5 %), or
- Sodium chloride 9 mg/ml (0.9 %) and Glucose 50 mg/ml (5 %) solution

Use -Luer-lock fittings on all syringes and sets. Large bore needles are recommended to minimise pressure and the possible formation of aerosols. The latter may also be reduced by the use of a venting needle.Administer the resulting solution over not less than 3 minutes via the tubing of a freely running intravenous infusion of the above fluids. Mitoxantrone should not be mixed with other drugs in the same infusion.

If extravasation occurs the administration should be stopped immediately and restarted in another vein.

b) Handling Cytotoxic drugs

Mitoxantrone, in common with other potentially hazardous cytotoxic drugs, should only be handled by adequately trained personnel. Pregnant staff should notbe involved in the reconstitution or administration of Mitoxantrone.

Care should be taken to avoid contact of Mitoxantrone with the skin, mucous membranes, or eyes. The use of goggles, gloves and protective gowns isrecommended during preparation, administration and disposal and the work surface should be covered with disposable plastic-backed absorbent paper.

Aerosol generation should be minimised. Mitoxantrone can cause staining. Skin accidentally exposed to Mitoxantrone should be rinsed copiously with warmwater and if the eyes are involved standard irrigation techniques should be used.

c) Spillage disposal

The following clean-up procedure is recommended if Mitoxantrone is spilled on equipment or environmental surfaces.Prepare a 50% solution of fresh concentrated bleach (any recognised proprietary brand containing either sodium or calcium hypochlorite) in water. Wetabsorbent tissues in the bleach solution and apply the wetted tissues to the spillage. The spillage is deactivated when the blue colour has been fullydischarged. Collect up the tissues with dry tissues. Appropriate protective equipmentshould be worn during the clean-up procedure.

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

All Mitoxantrone contaminated items (e.g. syringes, needles, tissues etc.) should be treated as toxic wasteand disposed of accordingly. Incineration is recommended.

7 MARKETING AUTHORISATION HOLDER

Generics (UK) Limited
Station Close
Potters Bar
Hertfordshire EN6 1TL
UK

8 MARKETING AUTHORISATION NUMBER

PA0405/084/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 31st May 2013

10 DATE OF REVISION OF THE TEXT

November 2015