
1.3.1.1 Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

Mitoxantron Accord 2 mg/ml, concentrate for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml concentrate for solution for infusion contains 2 mg mitoxantrone (as hydrochloride)

1 vial with 5 ml concentrate for solution for infusion contains 10 mg mitoxantrone (as hydrochloride)

1 vial with 10 ml concentrate for solution for infusion contains 20 mg mitoxantrone (as hydrochloride)

1 vial with 12.5 ml concentrate for solution for infusion contains 25 mg mitoxantrone (as hydrochloride)

1 vial with 15 ml concentrate for solution for infusion contains 30 mg mitoxantrone (as hydrochloride)

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for solution for infusion.

Appearance: Dark blue solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Mitoxantron Accord is indicated for the treatment of metastatic breast cancer, non-Hodgkin's lymphoma and acute non-lymphocytic leukaemia in adults, alone or in combination with other antineoplastic agents.

In the treatment of pain as a result of an advanced hormone-refractory prostate cancer in combination with a low dose of corticosteroids if the standard treatment with analgesic treatment is insufficient or inappropriate.

4.2 Posology and method of administration

Adults and the elderly:

Metastatic breast cancer, non-Hodgkin's lymphoma:

Monotherapy: The recommended starting dose of mitoxantrone in monotherapy is 14 mg/m² body surface area, administered in a single intravenous dose. This complete dose can be administered 21 days after the previous administration if the number of leukocytes and platelets has reached an acceptable level. In patients with an inadequate bone marrow reserve, for example as a consequence of previous chemotherapy or of a poor general condition, a lower starting dose (12 mg/m² or less) is recommended.

Adjustment of the dose and the frequency of subsequent administrations must be determined on the basis of the clinical assessment, depending on the extent and duration of the bone marrow suppression. Mitoxantrone must not be administered to patients in whom the number of neutrophils is <1,500/mm³ and/or platelets <25,000/mm³. The table below is presented as a guide for dose adjustment in the treatment of advanced breast cancer and non-Hodgkin's lymphoma, based on the haematological nadir (usually ten days after administration).

Nadir after earlier dose			
Leukocytes* (per mm³)	Platelets * (per mm³)	Time to recovery	Subsequent administration after an adequate haematological recovery
> 1,500	AND > 50,000	≤ 21 days	Repeat prior dose after recovery
> 1,500	AND > 50,000	> 21 days	Wait until recovery and then repeat the prior dose.
< 1,500	OR < 50,000	Undeter- mined	Reduce the prior dose by 2 mg/m ² after recovery
< 1,000	OR < 25,000	Undeter- mined	Reduce the prior dose by 4 mg/m ² after recovery.

Combination therapy: mitoxantrone has been administered as a component of a combination therapy. In cases of metastatic breast cancer, combinations of mitoxantrone with other cytotoxic 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 with another bone marrow suppressant, the starting dose of mitoxantrone should be 2 to 4 mg/m² less than the dose recommended for use in monotherapy. As indicated in the table above, subsequent administration is dependent on the severity and the duration of bone marrow suppression.

Acute non-lymphocytic leukaemia:

Administration in monotherapy in the event of recurrence: The recommended dose for remission induction is 12 mg/m² body surface area administered in a single intravenous dose per day for 5 consecutive days (total 60 mg/m²). In clinical studies with a dose of 12 mg/m² per day for 5 days in patients who achieved complete remission, this remission was the result of the first induction treatment.

Pain relief in hormone-refractory prostate carcinoma:

12 mg/m² administered as a short intravenous infusion with intervals of 21 days in combination with previous orally administered 10 mg prednisolone.

The table below is suggested as a guide for dose adjustment for pain relief of hormone-refractory prostate carcinoma.

Blood cell counts just before the next administration:

Leukocytes	Granulocytes	Platelets	Dose adjustment during the following course
> 3 x 10 ⁹ /l and	> 1.5 x 10 ⁹ /l and	>150 x 10 ⁹ /l	No dose adjustment
< 3 x 10 ⁹ /l or	< 1.5 x 10 ⁹ /l or	< 150 x 10 ⁹ /l	Delay the following course by intervals of one week until the required counts have been reached.

Blood cell counts at the nadir (10-14 days after administration)

Granulocytes	Platelets	Dose adjustment during the following course
< 0.5 x 10 ⁹ /l or	< 50 x 10 ⁹ /l	Reduce the dose by 2 mg/m ²
> 1.0 x 10 ⁹ /l and	> 100 x 10 ⁹ /l	In minimal non-haematological toxicity: increase the dose by 2 mg/m ²

Combination therapy: Mitoxantrone is used in combination therapy for the treatment of ANLL. Most clinical experience has been obtained with mitoxantrone in combination with cytarabine. This combination has been successfully used for the primary treatment of ANLL as well as for the treatment of recurrences.

An effective induction therapy in previously untreated patients consisted of mitoxantrone 10-12 mg/m² IV for 3 days in combination with cytarabine 100 mg/m² IV for 7 days (in continuous infusion). This was followed by a second induction and consolidation courses at the discretion of the treating physician. In clinical studies the duration of the treatment in induction and consolidation courses with mitoxantrone could be reduced to 2 days and that of cytarabine to 5 days. The above treatment regimen must also be adjusted by the treating physician depending on the individual characteristics of the patient.

Effectiveness has also been demonstrated with mitoxantrone in combination with etoposide in patients who showed signs of recurrence or who were refractory to a primary conventional chemotherapy. The use of mitoxantrone in combination with etoposide, as with other cytotoxic agents, can lead to greater myelosuppression than with mitoxantrone alone.

The dose adjustments must be made by the treating physician if necessary, taking account of the toxicity, the response and the individual characteristics of the patient.

In patients with renal disease caution is required (see Section 5.2. Pharmacokinetic properties).

For information about specific dosage regimens, please refer to the published literature.

Children and adolescents

As experience with mitoxantrone for treatment of leukaemia in children is limited, no dosage recommendations can currently be given for this patient population.

Route of administration

For intravenous use only.

The medicinal product must be diluted before use (see section 6.6. Instructions for use, handling and disposal).

One should avoid mitoxantrone coming into contact with the skin, the mucous membranes or the eyes.

If extravasation occurs, the infusion must be halted immediately and restarted in another vein. The non-blister-forming properties of mitoxantrone minimise the risk of severe local reactions as a result of extravasation.

See Section 6.2. Incompatibilities – 6.6. Instructions for use, handling and disposal.

4.3 Contraindications

Use in patients with severe myelosuppression

Hypersensitivity to mitoxantrone or to any of the excipients.

Lactation (for pregnancy see 4.6 Pregnancy and lactation).

Not for intrathecal use.

Not for intra-arterial use.

4.4 Special warnings and precautions for use

Mitoxantrone is an active cytotoxic agent which must be used under the supervision of a specialist oncologist with access to adequate facilities for monitoring of the clinical and laboratory parameters during and after the treatment. As with other cytotoxic agents, caution is required when handling mitoxantrone.

During the treatment, regular monitoring of clinical, haematological and biochemical parameters is necessary. A full blood count must be regularly performed during the course of treatment. On the basis of the values obtained, dose adjustments may be necessary (see Section 4.2. Posology and method of administration).

Mitoxantron Accord is not indicated for subcutaneous, intramuscular or intra-arterial injection. There have been reports of local/regional neuropathy, some irreversible, after an intra-arterial injection.

Mitoxantron Accord should not be administered as an intrathecal injection. There have been reports of neuropathy and neurotoxicity, both central and peripheral, after an intrathecal injection. These reports include cases leading to coma and severe neurological consequences, and paralysis with bladder and intestinal dysfunction.

In pancytopenia and severe wound infections, caution is advised if mitoxantrone is used.

Infections should be treated before starting treatment with mitoxantrone.

Mitoxantrone must be used with caution in patients with myelosuppression or in a poor general condition. More frequent blood counts are recommended, and in particular attention should be paid to neutrophils. Myelosuppression may be more severe and last longer in patients who have previously received extensive chemotherapy or radiotherapy or in weakened patients.

Cases of functional heart disorders have been described, including congestive heart failure and reduced left ventricular ejection fraction. Most of these heart disorders occurred in patients who had previously been treated with anthracycline derivatives, after prior radiotherapy of the mediastinum or of the thorax, or with a pre-existing heart condition. It is recommended that patients in this category should be treated with the full cytotoxic dose and the full regimen of mitoxantrone. In these patients, even greater caution is required and regular careful cardiac investigations are recommended from the start of the treatment. Particular caution must be exercised in patients who have previously been treated with a maximum cumulative dose of anthracyclines (e.g. doxorubicin and daunorubicin).

Given that experience of long-term treatment with mitoxantrone is currently limited, it is recommended that cardiac investigations should be carried out during treatment with a cumulative dose of more than 160 mg/m², even in patients without identifiable risk factors.

Careful supervision is recommended when treating patients with severe liver failure, oedema, ascites or pleural effusion.

For the population with liver failure, caution must be exercised, see section 4.2. Posology and method of administration and 5.2. Pharmacokinetic properties.

The sodium content per injection:
10 mg/5 ml: 0.739 mmol sodium and
20 mg/10 ml: 1.478 mmol.

This should be taken into account in patients on a restricted sodium diet.

Mitoxantrone can cause a blue-green discolouration of the urine 24 hours after administration and patients must be informed that this is to be expected.

Blue discolouration of the skin and nails has been reported occasionally. In very rare cases a reversible blue discolouration of the sclerae may occur.

In the treatment of leukaemia, hyperuricaemia can occur as a result of the rapid lysis of tumour cells by mitoxantrone. Monitor uric acid levels and initiate treatment to reduce uric acid before starting the anti-leukaemia treatment. Systemic infections must be treated at the same time or immediately before the start of mitoxantrone administration.

There is no experience with administration of mitoxantrone other than intravenous administration. The safety of intrathecal use has not been determined.

Immunisation can be ineffective if it is administered during treatment with mitoxantrone. Avoid immunisation with living virus vaccines.

Women of childbearing potential and their partners must be advised to avoid pregnancy and to use effective contraception during the treatment and for at least 6 months after discontinuing the treatment (see 4.6. Pregnancy and lactation).

4.5 Interaction with other medicinal products and other forms of interaction

Mitoxantrone in combination with other myelosuppressive drugs may increase the myelotoxicity of mitoxantrone and/or that of the concomitant drugs.

The combination of mitoxantrone with potentially cardiotoxic agents (e.g. other anthracyclines) increases cardiac toxicity.

Topoisomerase II inhibitors, including mitoxantrone, in combination with other antineoplastic agents and/or radiotherapy, have been associated with the onset of acute myeloid leukaemia (AML) or myelodysplastic syndrome (MDS) (see also section 4.8. Undesirable effects).

Immunisation can be ineffective if it is carried out during the treatment with mitoxantrone.

4.6 Fertility, pregnancy and lactation

Mitoxantrone can be genotoxic. Men who are treated with mitoxantrone are therefore advised not to father a child during treatment and for up to 6 months afterwards. In addition, it is advisable to obtain advice about freezing sperm before treatment due to the possibility of irreversible infertility as a result of the treatment with mitoxantrone. There are no adequate and well-controlled studies in pregnant women. The preclinical studies provided data in connection with reproductive toxicity, mutagenicity and carcinogenicity (see section 5.3 "Preclinical safety data") which indicate a potential risk for humans. Animal studies are inadequate with respect to teratogenicity and the potential risk for humans is unknown. Mitoxantrone must not be used in patients who are pregnant, in particular during the first trimester of pregnancy. If the medicinal product is used during pregnancy or if the patient becomes pregnant while she is using the medicinal product, the patient must be informed

about the potential risk for the foetus.

Women of childbearing potential and their partners must be advised to avoid a pregnancy and to use effective contraception during the treatment and for at least 6 months after discontinuation of treatment.

Mitoxantrone is excreted in breast milk and significant concentrations (18 mg/ml) have been reported during 28 days after the last administration. Because of the potential risk of severe side effects in the infant, mitoxantrone is contraindicated during breastfeeding (see section 4.3. Contraindications). Breastfeeding must be discontinued before treatment is started.

Breastfeeding is contraindicated. (see section 4.3)

4.7 Effects on ability to drive and use machines

Because of the possible side effects, mitoxantrone can influence the ability to drive and use machines.

4.8 Undesirable effects

Frequencies are determined as follows:

Very common ($\geq 1/10$), common ($\geq 1/100$ and $< 1/10$), uncommon ($\geq 1/1000$ and $< 1/100$), rare ($\geq 1/10,000$ and $\leq 1/1000$), very rare ($\leq 1/10,000$), unknown (cannot be estimated from the available data).

More than 10% of the patients can exhibit undesirable effects.

Myelosuppression is a dose-limiting undesirable effect of mitoxantrone.

The myelosuppression can be more pronounced and longer-lasting in patients who have previously received chemotherapy or radiotherapy. If mitoxantrone is used in hormone-resistant prostate cancer a number of other haematological undesirable effects can occur (see the sub-section Blood and lymphatic system disorders).

In a randomised phase II study in which the dose of mitoxantrone was increased starting from a neutrophil count of $> 1000/\text{mm}^3$, WHO grade 4 neutropenia ($\text{ANC} < 500/\text{mm}^3$) was observed in 54% of the patients who received mitoxantrone and a low dose of prednisone. The mean dose was $12 \text{ mg}/\text{m}^2$ mitoxantrone; 36 of the 84 patients received more than $12 \text{ mg}/\text{m}^2$ mitoxantrone. In a separate randomised study in which patients were treated with $14 \text{ mg}/\text{m}^2$ mitoxantrone, grade 4 neutropenia was observed in 23% of the patients who received mitoxantrone and hydrocortisone. Neutropenic fever and infections occurred in both studies in patients who were treated with mitoxantrone and hydrocortisone. The incidence of infections was 17% in one of the studies and was 14% for fever without infection; in the other study systemic infections occurred in 10% of the cases, urine infections in 9%, skin infections in 5% and fever in 6%. In these studies platelet counts of $< 50,000/\text{m}^3$ were observed in 4 and 3% respectively of patients who received mitoxantrone and corticosteroids.

Infections and infestations

Very common: infections, infection of the upper airways, infection of the urinary tract.

Common: pneumonia, sepsis, rhinitis

Unknown: opportunistic infections

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

Unknown: acute leukaemia

Topo-isomerase II inhibitors, including mitoxantrone, in combination with other antineoplastic agents and/or radiotherapy are associated with the development of acute myeloid leukaemia

(AML) or a myelodysplastic syndrome (MDS) (see also section 4.5. Interaction with other medicinal products and other forms of interaction).

Blood and lymphatic system disorders:

Very common:

Neutropenia. Dose increase due to haematological rash around the nadir (see 4.2) led to grade 4 neutropenia in 54% of the patients. Neutropenic fever occurred in 14% of patients.

Myelosuppression, bone marrow hypoplasia

Transient leukopenia with the lowest value 10-13 days after the treatment (severe leukopenia in 6%), anaemia, granulocytopenia, abnormal leukocyte counts.

Common: thrombocytopenia of $<50 \times 10^9/l$ occurred in 4% of patients.

Immune system disorders:

Unknown: anaphylactic reactions (including anaphylactic shock).

Metabolism and nutrition disorders:

Common: anorexia (loss of appetite)

Unknown: Hyperuricaemia.

Psychiatric disorders:

Uncommon: Anxiety, confusion

Nervous system disorders:

Common: non-specific neurological side effects have been reported such as dizziness, somnolence, neuritis, convulsion and mild paraesthesia.

Headache.

Eye disorders:

Uncommon: Reversible blue discolouration of the sclera has been reported.

Unknown: Conjunctivitis.

Cardiac disorders:

Very common: transient ECG change after long-term treatment. Arrhythmias.

Common: asymptomatic reduced left ventricular ejection fraction (2.6% at a cumulative dose of 140 mg/m^2), heart failure, chest pain, congestive heart failure after long-term treatment (2.6% at a cumulative dose of 140 mg/m^2). Sinus bradycardia.

Cardiac function must be monitored in patients who receive a cumulative dose $>160 \text{ mg/m}^2$ mitoxantrone.

Patients who receive anthracyclines or other cardiotoxic oncolytics and/or mediastinal radiation in advance and who also suffer from an underlying cardiovascular disease have a higher risk of heart problems. From post-marketing reports cardiotoxicity appears in treatment with mitoxantrone at a cumulative dose of less than 100 mg/m^2 .

Unknown: Cardiomyopathy and myocardial infarction have been reported.

Vascular disorders:

Very common: haemorrhages.

Common: Hypotension

Respiratory, thoracic and mediastinal disorders:

Common: Rhinitis

Uncommon: Dyspnoea.

Gastrointestinal disorders:

Very common: mild nausea and vomiting in approximately 50% of patients (severe in 1%), stomatitis, diarrhoea, abdominal pain. Constipation, mucositis, taste disturbances.

Uncommon: gastrointestinal bleeding.

Unknown: pancreatitis

Hepatobiliary disorders:

Common: hepatotoxicity, elevated liver enzymes (ALAT)

Skin and subcutaneous tissue disorders:

Very common: Alopecia grade I-II in approximately 50% of patients (severe alopecia is rare).

Uncommon: Rash, erythema

Rare: Blue colouring of skin and nails.

Unknown: Nail abnormalities (e.g. onycholysis nail dystrophy), extravasation at the infusion site has been reported, which can lead to erythema, swelling, pain, burning skin and/or a blue discolouration of the skin. Extravasation can lead to tissue necrosis, as a result of which debridement and a skin transplant may be necessary.

Renal and urinary disorders:

Very common: elevated urea concentration in the blood

Common: Discolouration of the urine within 24 hours following administration.

Nephrotoxicity, elevated serum creatinine levels and elevated plasma levels of nitrogen.

Reproductive system and breast disorders:

Common: amenorrhoea (can last for some time and resembles early menopause)

General disorders and administration site conditions:

Very common: Fever

Common: fatigue, oedema.

Uncommon: Allergic reactions (e.g. exanthema, dyspnoea, hypotension)

Unknown: Phlebitis at the administration site has also been reported. Weakness.

Investigations:

Very rare: change in body weight.

Injury, poisoning and procedural complications

Unknown: bruises

Tumour lysis syndrome (characterised by hyperuricaemia, hyperkalaemia, hyperphosphataemia and hypocalcaemia) have been observed rarely during chemotherapy in monotherapy with mitoxantrone, as well as during combination chemotherapy.

In patients with leukaemia, the pattern of side effects is mostly comparable, although the frequency and the severity are more pronounced, especially of stomatitis and mucositis.

Two cases of sudden death have been described in patients with widespread sclerosis who were treated with mitoxantrone. It is unknown whether a causal relationship exists with the use of mitoxantrone.

4.9 Overdose

Haematopoietic, gastro-intestinal, hepatic or renal toxicity can occur, depending on the dose administered and the physical condition of the patient.

Exceptional cases of death occurred as a result of severe leukopenia with infection in patients who accidentally received an injection of a single bolus of mitoxantrone at doses which were more than 10 times higher than the recommended dose.

There is no specific antidote to mitoxantrone.

In cases of overdose, the patient must be closely monitored. Treatment must be symptomatic and supportive.

Mitoxantrone is extensively tissue-bound and it is unlikely that peritoneal dialysis or haemodialysis will be effective in treating overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anthracyclines and related compounds.

ATC code: L01D B07

Mitoxantrone is an anthracenedione derivative that binds to nuclear DNA. The exact mechanism of action has not been fully explained. The medicine has a cytotoxic effect on both proliferating and non-proliferating human cells in culture, which indicates that mitoxantrone is not cell cycle-specific.

Mitoxantrone can be administered together with a number of other cytostatic agents and glucocorticoids. An increased effect on the function of the bone marrow and the gastrointestinal mucosa has been seen, but are reversible in nature. This can be avoided by adequate dose adjustment. No unexpected or severe undesirable effects were reported with concomitant administration of other medicinal products.

5.2 Pharmacokinetic properties

Pharmacokinetic studies in patients following intravenous administration of mitoxantrone indicate plasma clearance in three phases.

The distribution into tissues occurs rapidly and is extensive.

Protein binding: mitoxantrone has a protein binding rate of approximately 78%.

Mitoxantrone is excreted via the kidneys and the hepatobiliary system. Only 20-32% of the administered dose was excreted within the first 5 days of administration (urine 6-11%, faeces 13-25%). Of the substance recovered in the urine, 65% was unchanged mitoxantrone and the remaining 35% consisted mainly of two inactive metabolites and their glucuronide conjugates. Approximately two-thirds is excreted on the first day.

Elimination of the medicinal product takes place slowly with a mean half life of 12 days (range 5-18 days) and persisting tissue concentrations. Comparable estimates of the half life were obtained from patients treated with a single dose of mitoxantrone every 21 days and from patients in whom administration lasted for 5 consecutive days every 21 days.

5.3 Preclinical safety data

Reproductive toxicology: The intravenous administration of mitoxantrone at doses of 0.05 times the dose in humans (in mg/m²) in the pregnant rat resulted in a low foetal birth weight and delayed development of the kidneys. In the rabbit, mitoxantrone caused cases of premature parturition at dosages of 0.01 times the dose in humans. Mitoxantrone had no side effects on male or female fertility in the rat.

Mutagenicity: Mitoxantrone was mutagenic in bacterial and mammalian test systems in vitro. Mitoxantrone had a clastogenic effect in the hepatocytes of the rat and the ovarian cells of the Chinese hamster in vitro, and in the bone marrow of the rat in vivo.

Carcinogenicity: The intravenous administration of mitoxantrone to rats and mice every 21 days resulted in an increased incidence of fibroma and tumours of the external auditory canal in rats and in hepatocellular adenoma in male mice at dosages which were 0.02 to 0.03 times the dose in humans (in mg/m²).

Animal data are too limited to be able to draw conclusions regarding teratogenicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride,
sodium acetate (E 262),
acetic acid (E 260),
water for injections.

6.2 Incompatibilities

The medicinal product must not be mixed with other medicinal products and must only be diluted in the diluents specified under section 6.6 “Special precautions for disposal and other handling”.

6.3 Shelf life

Unopened vial: 2 years.

From a microbiological point of view, the reconstituted medicinal 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 unless reconstitution has taken place in controlled and validated aseptic conditions. See section 6.6, “Special precautions for disposal and other handling”.

6.4 Special precautions for storage

Do not store above 25°C. Do not refrigerate or freeze.

6.5 Nature and contents of container

Pack sizes: 10 mg/5ml (vial size 5 ml);
20 mg/10 ml (vial size 10 ml /15ml);
25 mg/12.5 ml (vial size 15 ml);
30 mg/15 ml (vial size 20 ml).
1, 5, 10 vials

Not all pack sizes may be marketed

Nature of container: glass vials glass type I, double window style with bromobutyl rubber stoppers.

6.6 Special precautions for disposal and other handling

Mitoxantron Accord 2 mg/ml must be diluted in at least 50 ml of one of the following free-flowing intravenous infusions: sodium chloride 0.9% or glucose 5%.

Mitoxantrone must not be mixed with other medicinal products in the same infusion.

After dilution the solution for infusion must be visually inspected prior to use. Only clear solutions practically free from visible particles may be used.

Care must be taken to avoid Mitoxantron Accord 2 mg/ml coming into contact with the skin, the mucous membranes or the eyes. It is recommended that glasses, gloves and protective clothing be worn during preparation and administration. Mitoxantron Accord 2 mg/ml may cause staining. If the skin accidentally comes into contact with Mitoxantron Accord 2 mg/ml, it should be rinsed with copious amounts of warm water. The standard irrigation techniques apply for the eyes.

The following cleaning procedure is recommended if mitoxantrone is spilled on equipment or surrounding surfaces. Prepare a 50% solution of fresh concentrated bleach (*about 10-13% available chlorine*) (any recognised proprietary brand containing either sodium or calcium hypochlorite) in water. Wet absorbent tissues in the bleach solution and apply the wetted tissues to the spillage. The spillage is deactivated when the blue colour has completely disappeared. Mop up the tissues with dry tissues. Wash the area with water and soak up the water with dry tissues. Appropriate protective clothing should be worn during the cleaning procedure. All items contaminated with mitoxantrone (e.g. syringes, needles, tissues, etc.) must be treated as toxic waste and the appropriate guidelines must be followed. Incineration is recommended. The statement about safety equipment must be retained.

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

7. MARKETING AUTHORISATION HOLDER

Accord Healthcare Limited
Sage House, 319, Pinner Road,
North Harrow, Middlesex, HA1 4HF
United Kingdom

8. MARKETING AUTHORISATION NUMBER

RVG 26663

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

03.07.2003/15.10.2009

10. DATE OF REVISION OF THE TEXT
