Package leaflet: Information for the patient

Mitoxantrone 2 mg/ml concentrate for solution for infusion

The active substance is mitoxantrone (as hydrochloride)

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. WHAT MITOXANTRONE CONCENTRATE FOR SOLUTION FOR INFUSION IS AND WHAT IT IS USED FOR

Mitoxantrone belongs to the group of medicines known as antineoplastic or anti-cancer medicines. It also belongs to the subgroup of anti-cancer medicines called anthracyclines. Mitoxantrone prevents cancer cells from growing, as a result of which they eventually die. The medicine also suppresses the immune system and is used because of this effect to treat a specific form of multiple sclerosis when there are no alternative treatment options.

Mitoxantrone is used in the treatment of:
- advanced stage (metastatic form) of breast cancer;
- a form of lymph node cancer (non-Hodgkin's lymphoma);
- a cancer of the blood in which the bone marrow (the spongy tissue inside the large bones) makes too many white blood cells (acute myeloid leukaemia);
- a cancer of the white blood cells (chronic myeloid leukaemia) at a stage where it is difficult to control the number of white blood cells (blast crisis). Mitoxantrone is used in combination with other medicinal products in this indication;
- pain caused by prostate cancer at an advanced stage of prostate cancer in combination with corticosteroids;
- highly active relapsing multiple sclerosis associated with rapidly evolving disability where no alternative therapeutic options exist (see sections 2 and 3).

2. WHAT YOU NEED TO KNOW BEFORE YOU USE MITOXANTRONE CONCENTRATE FOR SOLUTION FOR INFUSION

Do not use Mitoxantrone Concentrate for Solution for Infusion

- if you are allergic to mitoxantrone or any of the other ingredients of this medicine (see section 6);
- if you are allergic to sulphite;
- if you have a form of asthma (bronchial asthma) with sulphite allergy;
- if you are breast-feeding (see section "pregnancy and breast-feeding").

For use as treatment of multiple sclerosis:

- if you are pregnant.

Warnings and precautions
Mitoxantrone should be administered under the supervision of a doctor experienced in the use of cancer medicines that are toxic to your cells (cytotoxic chemotherapy agents).
Mitoxantrone should be given by slow and freely flowing infusion into the vein.

Mitoxantrone must not be administered under the skin (subcutaneous), in a muscle (intramuscular), or into the artery (intra-arterial). Severe local tissue damage may occur if Mitoxantrone leaks in surrounding tissue (extravasation) during administration.

Mitoxantrone must also not be injected into the space under the brain or spinal cord (intrathecal injection) as this can result in severe injury with permanent impairment.

Talk to your doctor or, pharmacist or nurse before using Mitoxantrone:
- if you have liver problems;
- if you have kidney problems;
- if you have used mitoxantrone before;
- if your heart is not working well;
- if you had prior radiotherapy of the chest;
- if you already use other medicines that affect your heart;
- if you had previous therapies with anthracyclines or anthracenediones, such as daunorubicin or doxorubicin;
- if your bone marrow is not working well (is depressed) or if you are in generally poor health;
- if you have an infection. This infection should be treated before taking mitoxantrone;
- if you plan a vaccination or immunisation during treatment. Vaccinations and immunisations may not work during treatment with mitoxantrone and for 3 months after the end of treatment;
- if you are pregnant or if you and your partner are trying to become pregnant;
- if you are breast-feeding. You should stop breast-feeding before taking mitoxantrone.

Tell your doctor or pharmacist or nurse immediately if you get any of the following signs or symptoms during treatment with mitoxantrone:
- fever, infections, unexplained bleeding or bruising, weakness and easy fatigability;
- breathlessness (including breathlessness at night), cough, fluid retention (swelling) in the ankles or legs, heart fluttering (irregular heart beat). This may occur either during or months to years after therapy with mitoxantrone.

Your doctor may need to adjust your treatment or stop mitoxantrone temporarily or permanently.

Blood tests prior and during treatment with mitoxantrone
Mitoxantrone may affect your blood cell counts. Before you start mitoxantrone and during treatment, your doctor will do a blood test to count the number of your blood cells. Your doctor will carry out blood tests more often, in which he will in particular monitor the number of white blood cells (neutrophilic leucocytes) in the blood:
- if you have a low count of a specific type of white blood cells (neutrophils) (less than 1,500 cells/mm^3);
- if you use mitoxantrone in high doses (>14 mg/m^2 per day x 3 days).

Heart function tests prior and during treatment with mitoxantrone
Mitoxantrone may damage your heart and cause a deterioration of your heart function or in more severe cases heart failure. You are more prone to these side effects if you take higher doses of mitoxantrone or:

- if your heart is not working well;
- if you had prior treatment of the chest with radiation;
- if you already use other medicines that affect your heart;
- if you had previous therapies with anthracyclines or anthracenediones, such as daunorubicin or doxorubicin.

Your doctor will do heart function tests before you start mitoxantrone and at regular intervals during therapy. If you receive mitoxantrone to treat multiple sclerosis your doctor will test your heart function before the start of therapy, prior to each subsequent dose and yearly for up to 5 years after the end of therapy.

Acute myeloid leukaemia (AML) and Myelodysplastic syndrome
A group of anticancer medicines (topoisomerase II inhibitors), including mitoxantrone, may cause the following diseases when used alone but especially in combination with other chemotherapy and/or radiotherapy:

- cancer of white blood cells (acute myeloid leukaemia, AML)
- a bone marrow disorder that causes abnormally shaped blood cells and leads to leukaemia (myelodysplastic syndrome)

Discolouration of urine and other tissues
Mitoxantrone may cause a blue-green colouration to the urine for 24 hours after administration. A bluish disolouration of the whites of your eyes, skin and nails may also occur.

Contraception in men and women
Men must not father a child and should use contraceptive measures during and at least 6 months after therapy. Women of childbearing potential should have a negative pregnancy test prior to each dose, and use effective contraception during therapy and for at least 4 months after cessation of therapy. If this medicine is used during pregnancy or if you become pregnant while taking this medicine, inform your doctor as there may be risks to the foetus.

Fertility
This medicine might increase the risk for transitory or persistent absence of menstruation (amenorrhoea) in women of childbearing age.

Children and adolescents
There is little experience in children and adolescents.
Do not give this medicine to children and adolescents from birth up to age of 18 years as safety and efficacy in children and adolescents have not been established.

Other medicines and mitoxantrone
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. It is particularly important that you mention any of the following medicines.

Medicines which may increase the risk of side effects with mitoxantrone:

- Medicines that can damage your heart (e.g. anthracyclines).
- Medicines that suppress the bone marrow's production of blood cells and platelets (myelosuppressive agents).
- Medicines that suppress your immune system (immunosuppressive agents).
- Antivitamin K, in particular if you are taking mitoxantrone because you have cancer.

- Topoisomerase II inhibitors (a groups of anticancer medicines including mitoxantrone) in combination with other chemotherapy and/or radiotherapy. These can cause:
  - cancer of white blood cells (acute myeloid leukaemia, AML);
  - a bone marrow disorder that causes abnormally shaped blood cells and leads to leukaemia (myelodysplastic syndrome).

Ask your doctor or pharmacist if you are not sure whether your medicine is one of the medicines listed above.

These medicines should be used with care or may need to be avoided during your treatment with mitoxantrone. If you are taking any of these, your doctor might need to prescribe an alternative medicine for you.

You should also tell your doctor if you are already taking mitoxantrone and you are prescribed a new medicine that you have not already taken at the same time as mitoxantrone.

Vaccinations and immunisation (protection against the vaccination substances) may not work during treatment with mitoxantrone and for three months after the end of treatment.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before you are given this medicine.

Pregnancy
Mitoxantrone may cause damage to your unborn child. Therefore you should avoid becoming pregnant. Mitoxantrone must not be used during pregnancy for treatment of multiple sclerosis (specifically in the first three months of the pregnancy).
If you become pregnant during the treatment with mitoxantrone, you must tell your doctor immediately and stop treatment with mitoxantrone.
You should avoid becoming pregnant. Men must use an effective method of contraception during the treatment and for at least 6 months after discontinuing the treatment. Women of child-bearing potential should have a negative pregnancy test prior to each dose and must practise effective contraception for at least 4 months after stopping the treatment with mitoxantrone.

Breast-feeding
Mitoxantrone is secreted into breast milk and may cause serious adverse reactions in your baby. You must not breast-feed while using mitoxantrone and for up to one month after the last administration.

Fertility
Mitoxantrone might increase the risk for transient or persistent absence of menstruation (amenorrhoea) in women of childbearing age. Therefore you should talk to your doctor if you are planning to become pregnant in the future; your eggs may need to be frozen. In men, no data are available. However, in male animals, damage to the testes and decreased sperm counts were observed.

Driving and using machines
Mitoxantrone has a minor effect on your ability to drive and use machines. This is caused by possible side effects, such as confusion or feeling tired (see section 4).
If you suffer from these side effects, do not drive any vehicles and/or use any machines.

Important information about some of the ingredients of Mitoxantrone Concentrate for Solution for Infusion
This medicine contains sodium metabisulphite, which can cause an allergic type reaction (skin rash, swelling of eyelids, face or lips, or difficulty in breathing). This is rare but you may be more at risk if you suffer from allergies or asthma.

This medicine contains 1.4 mmol sodium per 10 ml vial. To be taken into consideration by patients on a controlled sodium diet.

3. HOW TO USE MITOXANTRONE CONCENTRATE FOR SOLUTION FOR INFUSION

Posology and method of administration
Mitoxantrone will be given to you under supervision of a doctor experienced in the use of cytotoxic chemotherapy agents. It must always be administered as an intravenous infusion (in a vein) and must always be diluted before. The infusion liquid can leak out of the vein into the tissue (extravasation). If this happens, the infusion must be stopped and restarted in another vein. You should avoid contact with mitoxantrone, especially with the skin, mucous membranes (moist body surfaces, such as the lining of the mouth) and eyes. The individual dose of mitoxantrone is calculated by your doctor. The recommended dose is based on your body surface area, which is calculated in square metres (m^2) using your height and weight. In addition your blood will be tested regularly during the treatment. The dosage of the medicine will be adjusted in accordance with the results of these tests.

The usual dose is:
Metastatic breast cancer, non-Hodgkin's lymphoma
If mitoxantrone is used alone:

The recommended initial dosage of mitoxantrone is 14 mg/m^2 of body surface area, given as a single intravenous dose, which may be repeated at 21-day intervals, if your blood values have returned to acceptable levels.

A lower initial dosage (12 mg/m^2 or less) is recommended in patients with low bone marrow reserves e.g. due to prior chemotherapy or poor general condition.

Your doctor will decide precisely which subsequent dosage you need.
For subsequent courses, the prior dose can usually be repeated if white blood cell and platelet counts have returned to normal levels after 21 days.

Combination therapy (if used with other agents)
Mitoxantrone has been given as part of combination therapy. In metastatic breast cancer, combinations of mitoxantrone with other cytotoxic agents including cyclophosphamide and 5-fluorouracil or methotrexate and mitomycin C have been shown to be effective.

Mitoxantrone has also been used in various combinations for non-Hodgkin's lymphoma; however, data are presently limited and specific regimens cannot be recommended.

As a guide, when mitoxantrone is used in combination chemotherapy, the initial dose of mitoxantrone should be reduced by 2-4 mg/m^2 below the doses recommended when mitoxantrone is used alone.

Acute myeloid leukaemia:
If used alone for recurrence (return of the cancer)

The recommended dosage for remission induction is 12 mg/m^2 of body surface area, given as a single intravenous dose daily for five consecutive days (total of 60 mg/m^2 per 5 days).

If used with other agents against cancer:
Your doctor will decide exactly what dosage you need. This dose might be adjusted if:

- The combination of medicines reduces the production of white and red blood cells as well as platelets in your bone marrow more than mitoxantrone used alone;
- If you have serious liver or kidney problems.

Treatment of blast crisis in (chronic) myeloid leukaemia
Used alone for recurrence
The recommended dosage in relapse is 10 to 12 mg/m^2 body surface area given as a single intravenous dose daily over 5 consecutive days (total of 50 to 60 mg/m^2).

Advanced castrate-resistant prostate cancer
The recommended dosage of mitoxantrone is 12 to 14 mg/m^2 given as a short intravenous infusion every 21 days, in combination with low oral doses of corticosteroids (hormonal medicines that suppress the immune system).

Multiple Sclerosis
Mitoxantrone will be given to you under the supervision of a doctor experienced in the use of cytotoxic chemotherapeutic agents for the treatment of multiple sclerosis.
The recommended dosage of mitoxantrone is usually 12 mg/m^2 body surface area given as a short (approximately 5 to 15 minutes) intravenous infusion that may be repeated every 1 to 3 months. The maximum lifetime cumulative dose should not exceed 72 mg/m^2.

If mitoxantrone is administered repeatedly, dosing adjustments should be guided by extent and duration of the reduction in the number of white and red blood cells as well as platelets in your blood.

Elderly patients
Elderly patient should receive doses at the low end of the dosing range due to possible reduced liver, kidney or heart function and of possible illness or treatment with other medicines.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them. The most serious side effects are damage to the heart (myocardial toxicity) and myelosuppression (reduced activity of the bone marrow).

Some side effects could be serious
If any of the following happen, tell the doctor immediately:
- If your skin becomes pale and you feel weak or experience sudden shortness of breath, this can be sign of a reduction in red blood cells.
- Unusual bruising or bleeding, such as coughing up blood, blood in your vomit or urine, or black stools (potential sign of platelet reduction).
- New or worsening breathing difficulties.
- Chest pain, breathlessness, changes in your heartbeat (fast or slow), fluid retention (swelling) in the ankles or legs (potential signs or symptoms of heart problems).
- Severe itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat

(which may cause difficulty in swallowing or breathing), or if you feel you like you are going to faint, these may be signs of severe allergic reaction.
- Fever or infections.

For patients being treated for cancer:

Very Common (may affect more than 1 in 10 people)
- Infections.
- Low number of red blood cells which can cause a feeling of tiredness and shortness of breath (anaemia). You may require a blood transfusion.
- Low number of special white blood cells (neutrophils and leukocytes).
- Nausea (feeling sick).
- Vomiting (being sick).
- Hair loss.

Common (may affect up to 1 in 10 people)
- Low level of platelets – which may cause bleeding or bruising.
- Low number of special white blood cells (granulocytes).
- Loss of appetite.
- Tiredness, weakness and lack of energy.
- Congestive heart failure (severe condition where the heart cannot anymore pump enough blood).
- Heart attack.
- Shortness of breath.
- Constipation.
- Diarrhoea.
- Inflammation of the mouth and lips.
- Fever.

Uncommon (may affect up to 1 in 100 people)
- Reduced activity of the bone marrow. Your bone marrow can be more depressed or be depressed for a longer period if you have had chemotherapy or radiotherapy.
- Insufficient production of bloods cells in the bone marrow (bone marrow failure).
- Abnormal number of white blood cells.
- Severe allergic reaction (anaphylactic reaction including anaphylactic shock) – you may experience a sudden itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing, and you may feel you are going to faint).
- Infections of the upper airways.
- Infections of the urinary tract.
- Blood poisoning (sepsis).
- Infections caused by microorganisms which do not normally cause diseases with a healthy immune system (opportunistic infections).
- Cancer of the white blood cells (acute myeloid leukaemia (AML)).
- Bone marrow abnormality which causes the formation of abnormal blood cells which leads to leukaemia (myelodysplastic syndrome (MDS)).
- Changes in weight.
- Metabolic disturbances (tumour lysis syndrome).
- Anxiety.
- Confusion.
- Headache.
- Tingling sensation.
- Irregular heart beat or slowed heart beat.
- Abnormal electrocardiogram.

- Reduction of the volume of blood that the left ventricle can pump, with no symptoms.
- Bruising.
- Heavy bleeding.
- Low blood pressure.
- Abdominal pain.
- Bleeding in your stomach or bowels, this may include blood in vomit, bleeding when emptying the bowels or black tarry stool.
- Mucosal inflammation.
- Inflammation of the pancreas.
- Liver abnormalities.
- Skin inflammations (erythema).
- Nail abnormalities (e.g. detachment of the nail from the nail bed, changes in nail texture and structure).
- Rash.
- Changes to the colour of the whites of the eyes.
- Skin discolouration.
- Leakage of fluid into surrounding tissue (extravasation):
  - Reddening (erythema).
  - Swelling.
  - Pain.
  - Burning feeling and/or discolouration of the skin.
  - Death of tissue cells which can lead to the need to remove dead cells and skin transplantation.
- Abnormal results of blood tests to check liver and kidney functions (raised aspartate aminotransferase levels, elevated creatinine and urea nitrogen concentration in the blood).
- Damage to the kidneys, causing swelling and weakness (nephropathy).
- Urine discolouration.
- Abnormal absence of menstruation (amenorrhoea).
- Swelling (oedema).
- Taste disturbances.

Rare (may affect up to 1 in 1,000 people)
- Lung inflammation (pneumonia).
- Damages to the heart muscle preventing it from pumping properly (cardiomyopathy).

Not known (frequency cannot be estimated from the available data)
- A disease affecting the lung which can cause dry cough, bulb-like fingertips and nails, tiredness and shortness of breath that occurs during or after physical activity (interstitial pneumonitis).

For patients being treated for Multiple Sclerosis:

Very Common (may affect more than 1 in 10 people)
- Infections, including infections of the upper airways and urinary tract.
- Nausea (feeling sick).
- Hair loss.
- Abnormal absence of menstruation (amenorrhea).

Common (may affect up to 1 in 10 people)
- Low number of red blood cells which can cause a feeling of tiredness and shortness of breath (anaemia). You may require a blood transfusion.
- Low number of special white blood cells (granulocytes and leukocytes).
- Constipation.
- Vomiting (being sick).

- Diarrhoea.
- Inflammation of the mouth and lips.
- Abnormal number of white blood cells.
- Headache.
- Irregular heart beat.
- Abnormal electrocardiogram.
- Reduction of the volume of blood that the left ventricle can pump, with no symptoms.
- Abnormal results of blood tests to check liver function (raised aspartate aminotransferase levels).

Uncommon (may affect up to 1 in 100 people)
- Lung inflammation (pneumonia).
- Blood poisoning (sepsis).
- Infections caused by microorganisms which do not normally cause diseases with a healthy immune system (opportunistic infections).
- Cancer of the white blood cells (acute myeloid leukaemia (AML)).
- A bone marrow abnormality which causes the formation of abnormal blood cells which leads to leukaemia (myelodysplastic syndrome (MDS)).
- Insufficient production of blood cells in the bone marrow (bone marrow failure).
- Reduced activity of the bone marrow. Your bone marrow can be more depressed or be depressed for a longer period if you have had chemotherapy or radiotherapy.
- Low level of platelets – which may cause bleeding or bruising.
- Low number of special white blood cells (neutrophils).
- Severe allergic reaction (anaphylactic reaction including anaphylactic shock) – you may experience a sudden itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing, and you may feel you are going to faint).
- Loss of appetite.
- Changes in weight.
- Anxiety.
- Confusion.
- Tingling sensation.
- Tiredness, feeling weak and having no energy.
- Severe condition where the heart cannot anymore pump enough blood (congestive heart failure).
- Damages to the heart muscle preventing it from pumping properly (cardiomyopathy).
- Slowed heart beat.
- Heart attack.
- Unusual bruising.
- Heavy bleeding.
- Low blood pressure.
- Shortness of breath.
- Abdominal pain.
- Bleeding in your stomach or bowels, this may include blood in vomit, bleeding when emptying the bowels or black tarry stool.
- Mucosal inflammation.
- Inflammation of the pancreas.
- Liver abnormalities.
- Nail abnormalities (e.g. detachment of the nail from the nail bed, changes in nail texture and structure).
- Rash.
- Changes to the colour of the whites of the eyes.
- Skin discolouration.

- Leakage of fluid into surrounding tissue (extravasation):
  - Reddening (erythema).
  - Swelling.
  - Pain.
  - Burning feeling and/or discolouration of the skin.
  - Death of tissue cells which can lead to the need to remove dead cells and skin transplantation.
- Abnormal results of blood tests to check liver and kidney functions (elevated creatinine and urea nitrogen concentration in the blood).
- Damage to the kidneys, causing swelling and weakness (nephropathy).
- Urine discolouration.
- Swelling (oedema).
- Fever.
- Sudden death.

Rare (may affect up to 1 in 1,000 people)
None.

Not known (frequency cannot be estimated from the available data)
- A disease affecting the lung which can cause dry cough, bulb-like fingertips and nails, tiredness and shortness of breath that occurs during or after physical activity (interstitial pneumonitis).

Reporting of side effects

If you get any side effects, talk to your doctor or, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.
You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie.
By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE MITOXANTRONE CONCENTRATE FOR SOLUTION FOR INFUSION

Do not store above 25°C. Do not refrigerate or freeze
This medicine will be prepared and administered to you by healthcare staff. Any unused medicine must be disposed of by the healthcare staff.
Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label. The expiry date refers to the last day of that month.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Mitoxantrone Concentrate for Solution for Infusion contains

- The active substance is mitoxantrone (as hydrochloride).
- The other ingredients are glacial acetic acid, sodium acetate trihydrate, sodium chloride, sodium metabisulphite (E223) and Water for Injections.

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

What Mitoxantrone Concentrate for Solution for Infusion looks like and contents of the pack

This medicinal product is an anti-cancer medicine, in the form of a concentrate for solution for infusion (concentrated solution which is diluted to make a solution which can be given as a slow injection via a drip).
Mitoxantrone Concentrate for Solution for Infusion is a clear, dark blue solution.
It is available in packs containing 1 vial.

Important information about some of the ingredients of Mitoxantrone Concentrate for Solution for Infusion
This medicine contains sodium metabisulphite, which can cause an allergic type reaction (skin rash, swelling of eyelids, face or lips, or difficulty in breathing). This is rare but you may be more at risk if you suffer from allergies or asthma.

This medicine contains 1.4 mmol sodium per 10 ml vial. To be taken into consideration by patients on a controlled sodium diet.

Marketing Authorisation Holder
Pfizer Healthcare Ireland
9 Riverwalk, National Digital Park
Citywest Business Campus
Dublin 24, Ireland

Manufacturer
Pfizer Service Company BVBA, Hoge Wei 10, 1930 Zaventem, Belgium

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Other sources of information

Detailed information on this medicine is available on the website of the HPRA

The following information is intended for medical or healthcare professionals only:

Single use only. Discard any unused contents. Any unused product or waste materials should be disposed of in accordance with local requirements.

Mitoxantrone, in common with other potentially hazardous cytotoxic drugs, should only be handled by adequately trained personnel. Pregnant staff should not be 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 is recommended 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 warm water and if the eyes are involved standard irrigation techniques should be used.

Instructions for dilution and administration

FOR INTRAVENOUS USE ONLY.

Mitoxantrone should be given by intravenous infusion.

Syringes containing this product should be labelled 'MITOXANTRONE, FOR INTRAVENOUS USE ONLY.

Care should be taken to avoid contact of mitoxantrone with skin, mucous membranes or eyes.

Dilute the required volume of Mitoxantrone Concentrate for Solution for Infusion to at least 50 ml in either of the following infusion solutions: sodium chloride 0.9%, glucose 5%, or sodium chloride 0.18% and glucose 4%. 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. The non-vesicant properties of mitoxantrone minimise the risk of severe local reaction following extravasation.

Spillage disposal: The following clean-up procedure is recommended if Mitoxantrone Concentrate for Solution for Infusion 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. Wet absorbent tissues in the bleach solution and apply the wetted tissues to the spillage. The spillage is deactivated when the blue colour has been fully discharged. Collect up the tissues with dry tissues. Wash the area with water and soak up the water with dry tissues. Appropriate protective equipment should be worn during the clean-up procedure. All mitoxantrone contaminated items (e.g. syringes, needles, tissues etc.) should be treated as toxic waste and disposed of accordingly. Incineration is recommended.

Storage

As packaged for sale
Do not store above 25°C. Do not refrigerate or freeze.

In use
Mitoxantrone Sterile Concentrate does not contain an antimicrobial preservative.

Chemical and physical stability of the diluted product has been demonstrated for 72 hours when stored at room temperature.

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^{o}C, unless dilution has taken place in controlled and validated aseptic conditions.