Mitoxantrone “Ebewe” 2 mg/ml concentrate for solution for infusion

COMPOSITION

Each vial contains: 10 mg mitoxantrone (as hydrochloride)

CLINICAL PARTICULARS

Therapeutic Indications

Mitoxantrone hydrochloride is indicated only for the treatment of patients with progressive multiple sclerosis (i.e., patients whose neurological status is significantly abnormal between relapses) for whom additional therapy is indicated, and who have not been treated previously with mitoxantrone. Mitoxantrone “Ebewe” is not indicated in the treatment of patients with primary progressive multiple sclerosis.

Dosage and Method of Administration

Antileukaemic therapy: Mitoxantrone has been used in combination with other antileukaemic agents in the treatment of acute non-lymphocytic leukaemia (ANLL). The recommended dosage for patients with acute myeloid leukemia is 12 mg/m² given as a short intravenous infusion every 21 days. When used in combination with cytosine arabinoside (ARA-C) it is recommended that the dose of cytosine arabinoside be reduced to 2 days and that of cytosine arabinoside to 5 days. However, modification of the above regimen should not be undertaken without medical advice. Careful supervision is recommended when treating patients with severe hepatic insufficiency.

In cancer patients, symptomatic congestive heart failure (CHF) is known to occur in patients receiving up to 7 mg/m² of mitoxantrone. CHF has been reported in up to 2% of patients with chronic heart disease receiving mitoxantrone, and in up to 2% of patients with normal heart function receiving mitoxantrone. Mitoxantrone has been used safely in patients with baseline LVEF of <50% if the baseline ejection fraction have been reported. The majority of these cardiac events have occurred in patients who have had prior treatment with anthracycline derivatives, prior mediastinal/thoracic radiotherapy, or with doxorubicin. Mitoxantrone should not be given to patients with baseline neutrophil counts of less than 1,500 cells/mm3. In order to monitor for severe myelosuppression, patients should be started on mitoxantrone and treatment should be initiated before initiation of treatment for leukaemia.

As experience of prolonged treatment with mitoxantrone is presently limited, it is suggested that cardiac function be monitored at frequent intervals. A lower initial dosage (12 mg/m²) is recommended in patients with inadequate bone marrow reserves (i.e., patients who have received a cumulative life-time dose of >140 mg/m², or to those with either LVEF of <50% or a clinically significant reduction in LVEF.

Single-Agent Dosage in Relapse:

Acute Myeloid Leukaemia

The recommended dosage of mitoxantrone hydrochloride is 12 mg/m² body surface area given as a single intravenous dose for the consecutive days of 50 mg/m² (in clinical trials). If severe or life-threatening non-haematological toxicity is observed during the first induction course, the second induction course should be withheld until the toxicity clears. If severe or life-threatening non-haematological toxicity is observed during the first induction course, the second induction course should be withheld until the toxicity clears. If severe or life-threatening non-haematological toxicity is observed during the first induction course, the second induction course should be withheld until the toxicity clears.

Immunization may be ineffective when given during mitoxantrone therapy. Immunization with live-virus vaccines is therefore not recommended. Immunity to influenza vaccines is considered to be adequate. Mitoxantrone has been shown to cause the release of histamine from mast cells and basophils. Therefore, patients who have a history of hypersensitivity reactions to sulfites may be at risk for anaphylactic reactions.

Dose and schedule are based on weight and on cumulative dose. Mitoxantrone is contraindicated in patients with a history of allergic reactions to sulfites. Mitoxantrone is not indicated in the treatment of patients with primary progressive multiple sclerosis.

Prolonged Therapy: Mitoxantrone should be considered in the Treatment of Patients with Multiple Sclerosis

The recommended dosage of mitoxantrone hydrochloride is 12 mg/m² body surface area given as a single intravenous dose for the consecutive days of 50 mg/m² (in clinical trials). When used in combination with cytosine arabinoside (ARA-C) it is recommended that the dose of cytosine arabinoside be reduced to 2 days and that of cytosine arabinoside to 5 days. However, modification of the above regimen should not be undertaken without medical advice. Careful supervision is recommended when treating patients with severe hepatic insufficiency.

In cancer patients, symptomatic congestive heart failure (CHF) is known to occur in patients receiving up to 7 mg/m² of mitoxantrone. CHF has been reported in up to 2% of patients with chronic heart disease receiving mitoxantrone, and in up to 2% of patients with normal heart function receiving mitoxantrone. Mitoxantrone should not be given to patients with baseline neutrophil counts of less than 1,500 cells/mm³. In order to monitor for severe myelosuppression, patients should be started on mitoxantrone and treatment should be initiated before initiation of treatment for leukaemia.

As experience of prolonged treatment with mitoxantrone is presently limited, it is suggested that cardiac function be monitored at frequent intervals. A lower initial dosage (12 mg/m²) is recommended in patients with inadequate bone marrow reserves (i.e., patients who have received a cumulative life-time dose of >140 mg/m², or to those with either LVEF of <50% or a clinically significant reduction in LVEF.

Register the recommended initial dosage of mitoxantrone used as a single agent is 16 mg/m² of body surface area given as a single dose, but which may be repeated in 21 days in patients with a normal Previous Cardiac Risk Factors Report card.

The most common adverse effects of mitoxantrone are myelosuppression, nausea and vomiting, in conjunction with other antineoplastic therapy. As with other cytotoxic agents, caution should be exercised when combining mitoxantrone with other antineoplastic agents. As with other cytotoxic agents, caution should be exercised when combining mitoxantrone with other antineoplastic agents. As with other cytotoxic agents, caution should be exercised when combining mitoxantrone with other antineoplastic agents. As with other cytotoxic agents, caution should be exercised when combining mitoxantrone with other antineoplastic agents.

The toxicity of mitoxantrone is cumulative, and with a high incidence of severe and potentially lethal myelosuppression, mitoxantrone may not be considered appropriate for prolonged use beyond 3 courses. Mitoxantrone may be administered safely to patients with baseline LVEF of <50% if the baseline ejection fraction have been reported. The majority of these cardiac events have occurred in patients who have had prior treatment with anthracycline derivatives, prior mediastinal/thoracic radiotherapy, or with doxorubicin. Mitoxantrone should not be given to patients with baseline neutrophil counts of less than 1,500 cells/mm³. In order to monitor for severe myelosuppression, patients should be started on mitoxantrone and treatment should be initiated before initiation of treatment for leukaemia.

As experience of prolonged treatment with mitoxantrone is presently limited, it is suggested that cardiac function be monitored at frequent intervals. A lower initial dosage (12 mg/m²) is recommended in patients with inadequate bone marrow reserves (i.e., patients who have received a cumulative life-time dose of >140 mg/m², or to those with either LVEF of <50% or a clinically significant reduction in LVEF.

Evaluate the left-ventricular ejection fraction (LVEF) (by echocardiogram or MUGA) is recommended prior to administration of the initial dose of mitoxantrone hydrochloride and in the event that signs or symptoms of infection develop (see PRECAUTIONS).

Sulphite may cause allergic reactions including anaphylactic symptoms and bronchospasm in predisposed individuals. Mitoxantrone has been shown to cause the release of histamine from mast cells and basophils. Therefore, patients who have a history of hypersensitivity reactions to sulfites may be at risk for anaphylactic reactions.
A complete blood count, including platelets, should be obtained prior to each course of mitoxantrone HCl and in the event that signs and symptoms of infection develop. Mitoxantrone HCl generally should not be administered to patients who have severe neutropenia related to myelosuppression or to those with a history of severe infections. Leukopenia, which may be severe and related to myelosuppression, has been observed in patients receiving mitoxantrone HCl. 

Function tests should also be performed prior to each course of therapy. Mitoxantrone HCl therapy is contraindicated in patients with severe pre-existing liver disease. Additional care should be taken in patients with hepatic impairment as evidenced by abnormal liver function tests. Monitor liver function tests before each course of therapy and at least six months after cessation of therapy. Mitoxantrone should not normally be administered to patients with normal liver function tests who are confirmed to have a significantly abnormal liver test result. Mitoxantrone should not be administered to patients with recent or current hepatic disease, including hepatitis B or C or cirrhosis.

Instructions for Use, Handling and Disposal

Mitoxantrone HCl can be mixed with a number of other cytostatics and glucocorticoids. Mitoxantrone HCl can also be given concomitantly with other antineoplastic agents and/or radiotherapy, have been associated with the development of acute myeloid leukaemia (AML) or myelodysplastic syndrome (MDS). Interactions with Other Medicaments and Other Forms of Interaction Mitoxantrone HCl is partly cross-resistant to doxorubicin. Mitoxantrone HCl therapy is contraindicated in patients with a previous history of severe infections, including viral, bacterial, or fungal infections.

Topoisomerase II inhibitors, including mitoxantrone HCl, 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). Interactions with Other Medicaments and Other Forms of Interaction Mitoxantrone HCl is partly cross-resistant to doxorubicin. Mitoxantrone HCl therapy is contraindicated in patients with a previous history of severe infections, including viral, bacterial, or fungal infections.

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