4.2 Posology and Method of administration

**Epirubicin**

Concentrate for solution for infusion

**Epirubicin** 100 mg/m²                      **Cyclophosphamide** 500 mg/m²

Repeated every 28 days for 6 cycles

**Breast cancer** following regimens were used in trials supporting use of epirubicin as a single agent or in combination with other chemotherapeutic agents:

- Epirubicin 40 mg/m² on days 1-3, every 4 weeks
- Epirubicin 50 mg/m² on days 1-3, every 4 weeks
- Epirubicin 75 mg/m² on days 1, 2, 3, every 4 weeks

**Oncology**

For patients receiving a divided dose of epirubicin (Day 1 and Day 8). The Day 8 dose should be 75% of Day 1 if platelet counts are 75,000-100,000/mm³ and ANC is 1000 to 1499/mm³. If Day 8 platelet count is <75,000/mm³ and/or Day 8 ANC is <1000/mm³, the Day 8 dose should be cancelled and the Day 8 dose of epirubicin should be repeated on Day 15.

**Heart failure (New York Heart Association [NYHA] class II-IV)** has been reported in patients treated with anthracyclines, including epirubicin. For patients experiencing NYHA class II to IV heart failure, it should be treated with the standard medications for this purpose.

**4.5 Interactions with other medicinal products and other forms of treatment

Dexverapamil may alter the pharmacokinetics of epirubicin and is contraindicated for use with epirubicin.

**Effects at Site of Injection - Intra-arterial route -**

Injection may produce local pain, severe tissue lesions (vesication, necrosis, abscess formation). Blood vessel damage may lead to thrombosis.

**Intravesical use:**

Intravesical administration is not suitable for the treatment of bladder tumors.

**Concentration for solution for infusion:**

Injection is administered by intravenous infusion.

**4.2 Posology and Method of administration**

**Epirubicin** injection is administered to patients by intravenous infusion.

**4.4 Special warnings and special precautions for use**

**Breast cancer**

Standard doses of epirubicin in women with breast cancer are epirubicin 60-80 mg/m² every 4 weeks, with a dose interval of 4 to 6 weeks. Epirubicin should be administered as a single dose, followed by cyclophosphamide and 5-fluorouracil every 3 weeks.

**Oncology**

These regimens have been used in trials supporting use of epirubicin as a single agent or in combination with other chemotherapeutic agents:

- Epirubicin 40 mg/m² on days 1-3, every 4 weeks
- Epirubicin 50 mg/m² on days 1-3, every 4 weeks
- Epirubicin 75 mg/m² on days 1, 2, 3, every 4 weeks

For patients receiving a divided dose of epirubicin (Day 1 and Day 8). The Day 8 dose should be 75% of Day 1 if platelet counts are 75,000-100,000/mm³ and ANC is 1000 to 1499/mm³. If Day 8 platelet count is <75,000/mm³ and/or Day 8 ANC is <1000/mm³, the Day 8 dose should be cancelled and the Day 8 dose of epirubicin should be repeated on Day 15.

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**4.2 Posology and Method of administration**

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Dose Modifications

Dosage adjustments after the first treatment cycle should be made if the patient is experiencing during treatment cycle nadir platelet counts <50,000 mm³, ANC <1000/mm³, or Grade 3/4 nonhematologic toxicity. Recommended high starting dose (up to 120 mg/m²) should be administered on day 1, every 3 to 4 weeks. Patients with hepatocellular carcinoma may receive a bolus infusion of 90 mg/m². Epipodophyllotoxins are used in combination with other chemotherapy agents. If epirubicin is administered as a continuous infusion, this should be suspended if the patient develops a Grade 3-4 nonhematologic toxicity.

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Cardiac function monitoring must be particularly strict in patients treated with epirubicin, as it can cause cardiotoxicity. Repeated MUGA or ECHO determinations of LVEF should be performed, particularly with higher, cumulative anthracycline doses. The technique used for assessment should be consistent throughout follow-up.

Lactation

Epirubicin is excreted in human milk, and there are no appropriate data on the effects on the breastfed infant. Therefore, it is recommended that women do not breastfeed during treatment with epirubicin. No data are available on the effects of epirubicin on the neonate. Women who are pregnant or breastfeed should not be treated with epirubicin. Women of childbearing age must use adequate contraception during treatment and for at least 2 months after stopping treatment.

Cardiac monitoring of patients receiving epirubicin treatment is highly recommended. Patients must be carefully monitored. If signs of angina or cardiac ischaemia occur, the infusion must be stopped immediately. If epirubicin is administered as a continuous infusion, this should be suspended if the patient develops Grade 3/4 cardiotoxicity.

Investigations

The 4'-O-glucuronidation distinguishes epirubicin from doxorubicin and can explain the faster elimination of epirubicin and its reduced cardiotoxicity. Epirubicin has the potential to damage cardiac muscle fibers, leading to a decrease in cardiac output, which can be life-threatening. Patients with cardiac disease are at increased risk for developing cardiotoxicity with epirubicin.

Other -

Tumor-Lysis Syndrome -

5. ADVERSE REACTIONS

Acute overdosage with epirubicin will result in severe myelosuppression. There are no specific antidotes, and supportive care will be the treatment of choice. Epirubicin is excreted in human milk, and there are no appropriate data on the effects on the breastfed infant. Therefore, it is recommended that women do not breastfeed during treatment with epirubicin. No data are available on the effects of epirubicin on the neonate. Women who are pregnant or breastfeed should not be treated with epirubicin. Women of childbearing age must use adequate contraception during treatment and for at least 2 months after stopping treatment.

Gastrointestinal system -

Mucositis (can occur 5 to 10 days after treatment)

Mucositis

Mucositis/stomatitis generally appears early after drug administration and, if severe, may prevent the patient from continuing treatment. Epirubicin is emetigenic. Mucositis/stomatitis generally appears early after drug administration and, if severe, may prevent the patient from continuing treatment. Mucositis is one of the most common and dose-limiting toxicities of epirubicin.

Other -

Extrapulmonary Tumor Necrosis -

6. PHARMACEUTICAL PARTICULARS

Intravesical (transitional cell carcinoma, carcinoma in situ) and in the urinary tract, epirubicin has been administered in doses up to 25 mg/m² every 3 to 4 weeks. In patients with transitional cell carcinoma, a clinical benefit has been demonstrated with the intravesical administration of epirubicin. Epirubicin is not recommended for the treatment of breast cancer in combination therapy of anthracycline and dexrazoxane.

Investigations

Experimental data in animals suggest that epirubicin may cause fetal abnormalities (e.g., kidney malformations). Patients must be carefully monitored. If signs of angina or cardiac ischaemia occur, the infusion must be stopped immediately. If epirubicin is administered as a continuous infusion, this should be suspended if the patient develops Grade 3/4 cardiotoxicity.

Other -

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6. PHARMACEUTICAL PARTICULARS

Epirubicin may cause episodes of nausea and vomiting, diarrhea, and febrile neutropenia. Epirubicin can potentiate the effect of radiation to the mediastinal area. Epirubicin is excreted in human milk, and there are no appropriate data on the effects on the breastfed infant. Therefore, it is recommended that women do not breastfeed during treatment with epirubicin. No data are available on the effects of epirubicin on the neonate. Women who are pregnant or breastfeed should not be treated with epirubicin. Women of childbearing age must use adequate contraception during treatment and for at least 2 months after stopping treatment.

Gastrointestinal system -

Mucositis (can occur 5 to 10 days after treatment)

Tumor-Lysis Syndrome -

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