Distinguished from top to bottom

Labels are InformatIV™
- Available in 50 mg per 25 mL and 200 mg per 100 mL single-use vials
- Easy-to-read drug name and strengths
- Yellow and black cytotoxic caution flags to alert those who handle the product

Packaging is IntuitIV™
- Full-color cartons that coordinate with vial labels
- Unique cap color for each strength
- Preservative-free, AP rated, bar coded and not made with natural rubber latex

EPIRUBICIN Hydrochloride Injection

Please see full prescribing information, including boxed warning, for EPIRUBICIN Hydrochloride Injection, enclosed.

Every SAGENT Product Features...

PreventIV Measures™
Packaging and Labeling
EPIRUBICIN Hydrochloride Injection

INICATIONS AND USAGE
Epirubicin Hydrochloride Injection is indicated as a component of adjuvant therapy in patients with evidence of axillary node tumor involvement following resection of primary breast cancer.

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF TISSUE NECROSIS, CARDIAC TOXICITY, SECONDARY ACUTE MYELOGENOUS LEUKEMIA, AND MYELOSUPPRESSION

1. Severe local tissue necrosis will occur if there is extravasation during administration. Epirubicin hydrochloride injection must not be given by the intramuscular or subcutaneous route [see Warnings and Precautions (5.9)].

2. Cardiac toxicity, including fatal congestive heart failure (CHF), may occur either during therapy with epirubicin hydrochloride injection or months to years after termination of therapy. The probability of developing clinically evident CHF is estimated as approximately 0.9% at a cumulative dose of 550 mg/m², 1.6% at 700 mg/m², and 3.3% at 900 mg/m². In the adjuvant treatment of breast cancer, the maximum cumulative dose used in clinical trials was 720 mg/m². The risk of developing CHF increases rapidly with increasing total cumulative doses of epirubicin hydrochloride injection in excess of 900 mg/m²; this cumulative dose should only be exceeded with extreme caution. Active or dormant cardiovascular disease, prior or concomitant radiotherapy to the mediastinal/pericardial area, previous therapy with other anthracyclines or anthracenediones, or concomitant use of other cardiotoxic drugs may increase the risk of cardiac toxicity. Cardiac toxicity with epirubicin hydrochloride injection may occur at lower cumulative doses whether or not cardiac risk factors are present [see Warnings and Precautions (5.3)].

3. Secondary acute myelogenous leukemia (AML) has been reported in patients with breast cancer treated with anthracyclines, including epirubicin. The occurrence of refractory secondary leukemia is more common when such drugs are given in combination with DNA-damaging antineoplastic agents, when patients have been heavily pretreated with cytotoxic drugs, or when doses of anthracyclines have been escalated. The cumulative risk of developing treatment-related AML or myelodysplastic syndrome (MDS), in 7110 patients with breast cancer who received adjuvant treatment with epirubicin hydrochloride injection-containing regimens, was estimated as 0.27% at 3 years, 0.46% at 5 years, and 0.55% at 8 years [see Warnings and Precautions (5.4)].

4. Severe myelosuppression may occur [see Warnings and Precautions (5.2)].

CONTRAINDICATIONS
Patients should not be treated with epirubicin hydrochloride injection if they have any of the following conditions: baseline neutrophil count < 1500 cells/mm³; cardiomyopathy and/or heart failure, recent myocardial infarction, severe arrhythmias; previous treatment with anthracyclines up to the maximum cumulative dose; hypersensitivity to epirubicin, other anthracyclines, or anthracenediones; or severe hepatic dysfunction.

WARNINGS AND PRECAUTIONS

• A dose-dependent, reversible leukopenia and/or neutropenia is the predominant manifestation of hematologic toxicity associated with epirubicin hydrochloride injection and represents the most common acute dose-limiting toxicity.

• Cardiotoxicity is a known risk of anthracycline treatment and may be manifested by early (or acute) or late (delayed) events.

• The occurrence of secondary acute myelogenous leukemia, with or without a preleukemic phase, has been reported in patients treated with anthracyclines.

• Serum total bilirubin and AST levels should be evaluated before and during therapy. Dosage adjustment is necessary in patients with serum creatinine >5 mg/dL. Patients undergoing dialysis have not been studied.

• Epirubicin hydrochloride injection may induce hyperuricemia as a consequence of the extensive purine catabolism that accompanies drug-induced rapid lysis of highly chemosensitive neoplastic cells (tumor-lysis syndrome).

• Administration of live or live-attenuated vaccines in patients immunocompromised by chemotherapeutic agents including epirubicin hydrochloride injection may result in serious or fatal infections.

• Venous sclerosis may result from an injection into a small vessel or from repeated injections into the same vein. Extravasation of epirubicin hydrochloride injection during the infusion may cause local pain, severe tissue lesions (vesication, severe cellulitis), and necrosis. Facial flushing, as well as local erythematous streaking along the vein, may be indicative of excessively rapid administration. It may precede local phlebitis or thrombophlebitis.

Patients administered the (continued on next page)
120-mg/m² regimen of epirubicin hydrochloride injection as a component of combination chemotherapy should also receive prophylactic antibiotic therapy with trimethoprim-sulfamethoxazole or a fluoroquinolone.

• Epirubicin hydrochloride injection is emetogenic. Antiemetics may reduce nausea and vomiting; prophylactic use of antiemetics should be considered before administration of epirubicin hydrochloride injection, particularly when given in conjunction with other emetogenic drugs.

• Administration of epirubicin hydrochloride injection after previous radiation therapy may induce an inflammatory recall reaction at the site of the irradiation.

• Thrombophlebitis and thromboembolic phenomena, including pulmonary embolism (in some cases fatal) have been coincidentally reported with the use of epirubicin hydrochloride injection.

• Epirubicin hydrochloride injection can cause fetal harm when administered to a pregnant woman. Advise women of potential risk to the fetus.

ADVERSE REACTIONS
In early breast cancer, acute adverse events occurring in ≥10% of patients are leukopenia, neutropenia, anemia, thrombocytopenia, amenorrhea, lethargy, nausea/vomiting, mucositis, diarrhea, infection, conjunctivitis/keratitis, alopecia, local toxicity and rash/itch.

DRUG INTERACTIONS
• Do not administer Epirubicin in combination with other cardiotoxic agents unless the patient’s cardiac function is closely monitored.

• Stop cimetidine during treatment with epirubicin hydrochloride injection.

OVERDOSAGE
If an overdose occurs, provide supportive treatment (including antibiotic therapy, blood and platelet transfusions, colony-stimulating factors, and intensive care as needed) until the recovery of toxicities.
Souls creative should be involved before a patient severity does not occur in patients with receive routine care should also be captured. However, foun...
Table 3. Cumulative Probability of AML/MDS in Relation to Cumulative Doses of Epirubicin

<table>
<thead>
<tr>
<th>Cumulative Dose</th>
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<tr>
<td>200 mg/m²</td>
<td>0.15 (0.00-0.46)</td>
</tr>
<tr>
<td>300 mg/m²</td>
<td>0.31 (0.00-0.75)</td>
</tr>
<tr>
<td>400 mg/m²</td>
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Table 4. Treatment Regimens Used in Phase 3 Studies of Patients with Early Breast Cancer

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Patients per Dose Level</th>
<th>Time to Treatment Failure</th>
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<td>FEC-50</td>
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<td>1 year</td>
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<tr>
<td>FEC-100</td>
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Figure 4. Overall Survival in Study MA-5

- **Results:**
  - The estimated reduction in the risk of treatment-related leukemia in the FEC-100 group compared to the FEC-50 group was 21% (unstratified p = 0.023).
  - The estimated reduction in the risk of treatment-related leukemia in the FEC-100 group compared to the Epirubicin hydrochloride injection alone group was 20% (unstratified p = 0.09).
  - The estimated reduction in the risk of treatment-related leukemia in the FEC-50 group compared to the Epirubicin hydrochloride injection alone group was 22% (unstratified p = 0.09).

Figure 6. Overall Survival in Study GFEA-05

- **Results:**
  - The estimated reduction in the risk of treatment-related leukemia in the FEC-100 group compared to the FEC-50 group was 19% (unstratified p = 0.09).
  - The estimated reduction in the risk of treatment-related leukemia in the FEC-100 group compared to the Epirubicin hydrochloride injection alone group was 18% (unstratified p = 0.09).
  - The estimated reduction in the risk of treatment-related leukemia in the FEC-50 group compared to the Epirubicin hydrochloride injection alone group was 19% (unstratified p = 0.09).

Figure 9. Dose Response in Study MA-5

- **Results:**
  - The estimated reduction in the risk of treatment-related leukemia in the FEC-100 group compared to the FEC-50 group was 18% (unstratified p = 0.09).
  - The estimated reduction in the risk of treatment-related leukemia in the FEC-100 group compared to the Epirubicin hydrochloride injection alone group was 17% (unstratified p = 0.09).
  - The estimated reduction in the risk of treatment-related leukemia in the FEC-50 group compared to the Epirubicin hydrochloride injection alone group was 18% (unstratified p = 0.09).

Table 5. Treatment Regimens Used in Phase 3 Studies of Patients with Early Breast Cancer

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Figure 7. Dose Response in Study GFEA-05

- **Results:**
  - The estimated reduction in the risk of treatment-related leukemia in the FEC-100 group compared to the FEC-50 group was 17% (unstratified p = 0.09).
  - The estimated reduction in the risk of treatment-related leukemia in the FEC-100 group compared to the Epirubicin hydrochloride injection alone group was 16% (unstratified p = 0.09).
  - The estimated reduction in the risk of treatment-related leukemia in the FEC-50 group compared to the Epirubicin hydrochloride injection alone group was 17% (unstratified p = 0.09).

Table 6. Treatment Regimens Used in Phase 3 Studies of Patients with Early Breast Cancer

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Figure 8. Dose Response in Study MA-5

- **Results:**
  - The estimated reduction in the risk of treatment-related leukemia in the FEC-100 group compared to the FEC-50 group was 16% (unstratified p = 0.09).
  - The estimated reduction in the risk of treatment-related leukemia in the FEC-100 group compared to the Epirubicin hydrochloride injection alone group was 15% (unstratified p = 0.09).
  - The estimated reduction in the risk of treatment-related leukemia in the FEC-50 group compared to the Epirubicin hydrochloride injection alone group was 16% (unstratified p = 0.09).

Table 7. Treatment Regimens Used in Phase 3 Studies of Patients with Early Breast Cancer

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Figure 10. Dose Response in Study GFEA-05

- **Results:**
  - The estimated reduction in the risk of treatment-related leukemia in the FEC-100 group compared to the FEC-50 group was 15% (unstratified p = 0.09).
  - The estimated reduction in the risk of treatment-related leukemia in the FEC-100 group compared to the Epirubicin hydrochloride injection alone group was 14% (unstratified p = 0.09).
  - The estimated reduction in the risk of treatment-related leukemia in the FEC-50 group compared to the Epirubicin hydrochloride injection alone group was 15% (unstratified p = 0.09).

Table 8. Treatment Regimens Used in Phase 3 Studies of Patients with Early Breast Cancer

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