

## **IDarubicin Hydrochloride** Injection **Antineoplastic Agent**

### SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form/ Strength	Clinically Relevant Nonmedicinal Ingredients
Intravenous injection	Solution for injection 1 mg/mL (5 mL, 10 mL and 20 mL vials)	<i>For a complete listing, see DOSAGE FORMS, COMPOSITION AND PACKAGING section.</i>

### INDICATIONS AND CLINICAL USE

Idarubicin Hydrochloride Injection alone or in combination chemotherapy regimens involving other cytotoxic agents, is indicated in:

- Acute non-lymphocytic leukemia (ANLL); in adults for remission induction as front-line therapy or for remission induction in relapsed or refractory patients.
- Acute lymphocytic leukemia (ALL) as second-line treatment in adults and children.

**Pediatrics:** Idarubicin Hydrochloride Injection is indicated in acute lymphocytic leukemia (ALL) as second-line treatment in children.

**Geriatrics (> 65 years of age):** Patients over 60 years of age who were undergoing induction therapy experienced congestive heart failure, serious arrhythmias, chest pain, myocardial infarction, and asymptomatic declines in LVEF more frequently than younger patients (see **WARNINGS AND PRECAUTIONS, DOSAGE AND ADMINISTRATION** and **ADVERSE REACTIONS**).

### CONTRAINDICATIONS

- Patients who are hypersensitive to idarubicin hydrochloride or to any ingredient in the formulation or component of the container. For a complete listing, see the **DOSAGE FORMS, COMPOSITION AND PACKAGING** section.
- Hypersensitivity to any other anthracyclines or anthracenediones such as epirubicin hydrochloride, daunorubicin hydrochloride, mitoxantrone or mitomycin C;
- Uncontrolled infections;
- Marked persistent myelosuppression induced by prior treatment with other antitumour agents or by radiotherapy;
- Severe hepatic impairment;
- Severe renal impairment;
- Severe myocardial insufficiency;
- Recent myocardial infarction;
- Severe arrhythmias;
- History of severe cardiac disease;
- Previous treatment with maximum cumulative doses of idarubicin, doxorubicin, daunorubicin, epirubicin and/or other anthracyclines and anthracenediones (see **WARNINGS AND PRECAUTIONS**).

### WARNINGS AND PRECAUTIONS

<p align="center"><b>Serious Warnings and Precautions</b></p> <p><b>IDARUBICIN HYDROCHLORIDE INJECTION is intended for use under the direction of physicians experienced in chemotherapy.</b></p> <ul style="list-style-type: none"> <li>• Myelosuppression (see <b>WARNINGS AND PRECAUTIONS, Hematologic</b>)</li> <li>• Cardiotoxicity (see <b>WARNINGS AND PRECAUTIONS, Cardiovascular</b>)</li> </ul>
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#### General

Therapy with idarubicin hydrochloride injection requires close observation of the patient and laboratory monitoring. Idarubicin hydrochloride may induce hyperuricemia as a consequence of the extensive purine catabolism that accompanies drug-induced rapid lysis of neoplastic cells ("tumor lysis syndrome"). Blood uric acid levels, potassium, calcium, phosphate, and creatinine should be evaluated after initial treatment. Hydration, urine alkalinization, and prophylaxis with allopurinol to prevent hyperuricemia

may minimize potential complications of tumor lysis syndrome. Appropriate measures must be taken to control any systemic infection before beginning therapy.

Patients should recover from acute toxicities of prior cytotoxic treatment (such as stomatitis, neutropenia, thrombocytopenia, and generalized infections) before beginning treatment with idarubicin.

Extravasation of idarubicin hydrochloride injection at the site of intravenous injection can cause severe local tissue necrosis. The risk of thrombophlebitis at the injection site may be minimized by following the recommended procedure for administration.

#### Carcinogenesis and Mutagenesis

Like most other cytotoxic agents, idarubicin has mutagenic properties.

Idarubicin was genotoxic in most of the *in vitro* or *in vivo* tests performed. Intravenous idarubicin was carcinogenic, toxic to the reproductive organs, and embryotoxic and teratogenic in rats.

Idarubicin can induce chromosomal damage in human spermatozoa. For this reason, males undergoing idarubicin treatment should use contraceptive measures.

Secondary leukemia, with or without a preleukemic phase, has been reported in patients treated with anthracyclines, including idarubicin. Secondary leukemia is more common when such drugs are given in combination with DNA-damaging antineoplastic agents. These leukemias can have a 1- to 3-year latency period.

#### Cardiovascular

Cardiotoxicity is a risk of anthracycline treatment that may be manifested by early (i.e., acute) or late (i.e., delayed) events.

**Early (i.e., Acute) Events:** Early cardiotoxicity of idarubicin consists mainly of sinus tachycardia and/or ECG abnormalities, such as non-specific ST-T wave changes. Tachyarrhythmias, including premature ventricular contractions and ventricular tachycardia, bradycardia, as well as atrioventricular and bundle-branch block have also been reported. These effects do not usually predict subsequent development of delayed cardiotoxicity, are rarely of clinical importance, and are generally not a consideration for the discontinuation of idarubicin treatment. However, acute life-threatening arrhythmias have been occasionally observed during therapy. Subacute effects such as pericarditis/myocarditis have also been reported.

**Late (i.e., Delayed) Events:** Delayed cardiotoxicity usually develops late in the course of therapy or within 2 to 3 months after completion of treatment, but later events, several months to years after completion of treatment, have also been reported. Delayed cardiomyopathy is manifested by reduced left ventricular ejection fraction (LVEF) and/or signs and symptoms of congestive heart failure (CHF) such as dyspnea, pulmonary edema, dependent edema, cardiomegaly and hepatomegaly, oliguria, ascites, pleural effusion, and gallop rhythm. Subacute effects such as pericarditis/myocarditis have also been reported. Life-threatening CHF is the most severe form of anthracycline-induced cardiomyopathy and represents the cumulative dose-limiting toxicity of the drug.

Cumulative dose limits for i.v. or oral idarubicin have not been defined. **However, idarubicin-related cardiomyopathy was reported in 5% of patients who received cumulative i.v. doses of 150 to 290 mg/m<sup>2</sup>.** Available data on patients treated with oral idarubicin total cumulative doses up to 400 mg/m<sup>2</sup> suggest a low probability of cardiotoxicity.

Cardiac function should be assessed before patients undergo treatment with idarubicin and must be monitored throughout therapy to minimize the risk of incurring severe cardiac impairment. The risk may be decreased through regular monitoring of LVEF during the course of treatment with prompt discontinuation of idarubicin at the first sign of impaired function. The appropriate quantitative method for repeated assessment of cardiac function (evaluation of LVEF) includes multi-gated radionuclide angiography (MUGA) or echocardiography (ECHO). A baseline cardiac evaluation with an ECG and either a MUGA scan or an ECHO is recommended, especially in patients with risk factors for increased 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.

Risk factors for cardiac toxicity include active or dormant cardiovascular disease, prior or concomitant radiotherapy to the mediastinal/pericardial area, previous therapy with other anthracyclines or anthracenediones, and concomitant use of drugs with the ability to suppress cardiac contractility or cardiotoxic drugs. Anthracyclines including idarubicin should not be administered in combination with other cardiotoxic agents unless the patient's cardiac function is closely monitored.

Patients receiving anthracyclines after stopping treatment with other cardiotoxic agents, especially those with long half-lives such as trastuzumab, may also be at an increased risk of developing cardiotoxicity. The half-life of trastuzumab is approximately 28.5 days and may persist in the circulation for up to 24 weeks. Therefore, physicians should avoid anthracycline-based therapy for up to 24 weeks after stopping trastuzumab when possible. If anthracyclines are used before this time, careful monitoring of cardiac function is recommended.

Cardiac function monitoring must be particularly strict in patients receiving high cumulative doses and in those with risk factors. However, cardiotoxicity with idarubicin may also occur at lower cumulative doses whether or not cardiac risk factors are present.

Cardiac toxicity of the type described for other anthracycline compounds, manifested by clinically evident CHF or by a decrease in LVEF may occur during therapy or several weeks after termination of therapy. Discontinuation of idarubicin hydrochloride injection and treatment with vasodilators, diuretics, digitalis, sodium restriction and bed-rest are indicated.

In infants and children, there appears to be a greater susceptibility to anthracycline-induced cardiac toxicity, and a long-term periodic evaluation of cardiac function should be performed.

#### **Extravasation and Vascular Effects**

Extravasation of idarubicin hydrochloride injection during intravenous administration can cause local pain, severe tissue lesions (vesication, severe cellulitis) and severe local tissue necrosis. Extravasation may occur with or without an accompanying stinging or burning sensation even if blood returns well on aspiration of the infusion needle. If signs or symptoms of extravasation occur, the injection or infusion should be immediately stopped (see **DOSAGE AND ADMINISTRATION**).

Phlebosclerosis may result from an injection into a small vessel or from previous injections into the same vein. Following the recommended procedures may minimize the risk of phlebitis/thrombophlebitis at the injection site (see **DOSAGE AND ADMINISTRATION**).

As with other cytotoxic agents, thrombophlebitis and thromboembolic phenomena, including pulmonary embolism, have been coincidentally reported with the use of idarubicin.

#### **Gastrointestinal**

Idarubicin is emetogenic. Mucositis (mainly stomatitis, less often esophagitis) generally appears early after drug administration and, if severe, may progress over a few days to mucosal ulcerations. Most patients recover from this adverse event by the third week of therapy.

Occasionally, episodes of serious gastrointestinal events (such as perforation or bleeding) have been observed in patients receiving oral idarubicin who had acute leukemia or a history of other pathologies or had received medications known to lead to gastrointestinal complications. In patients with active gastrointestinal disease with increased risk of bleeding and/or perforation, the physician must balance the benefit of oral idarubicin therapy against the risk.

#### **Hematologic**

Idarubicin hydrochloride injection is a potent bone marrow suppressant. Myelosuppression primarily of leukocytes will therefore occur in all patients given a therapeutic dose of this agent. Hematologic profiles should be assessed before and during each cycle of therapy with idarubicin including differential white blood cell (WBC) counts. A dose-dependent reversible leukopenia and/or granulocytopenia (neutropenia) is the predominant manifestation of idarubicin hematologic toxicity and is the most common acute dose-limiting toxicity of this drug. Leukopenia and neutropenia are usually severe; thrombocytopenia and anemia may also occur. Neutrophil and platelet counts usually reach their nadir 10 to 14 days following administration; however cell counts generally return to normal levels during the third week. Clinical consequences of severe myelosuppression may be fever, infections, sepsis/septicemia, septic shock, hemorrhage, tissue hypoxia, or death. Facilities with laboratory and supportive resources adequate to monitor drug tolerability and protect and maintain a patient compromised by drug toxicity should be available. It must be possible to treat rapidly and completely a severe hemorrhagic condition and/or a severe infection.

#### **Hepatic/Biliary/Pancreatic**

Idarubicin hydrochloride injection therapy should not be administered in patients with severe liver impairment or in patients with uncontrolled infections unless the benefit outweighs the risk.

Since hepatic function impairment can affect the disposition of idarubicin, liver function should be evaluated with conventional clinical laboratory tests (using serum bilirubin as indicator) prior to and during treatment. In a number of Phase III clinical trials, treatment was not given if bilirubin serum levels exceeded 2 mg/dL. With other anthracyclines, a 50% dose reduction is generally employed if bilirubin levels exceed 40 µmol/L (2.35 mg/dL).

#### **Renal**

Idarubicin hydrochloride injection therapy should not be administered in patients with severe renal impairment.

Since renal function impairment can affect the disposition of idarubicin, kidney function should be evaluated with conventional clinical laboratory tests (using serum creatinine as indicator) prior to and during treatment. In a number of Phase III clinical trials, treatment was not given if creatinine serum levels exceeded 2 mg/dL. With other anthracyclines, a 50% dose reduction is generally employed if creatinine levels exceed 200 µmol/L (2.25 mg/dL).

#### **Immunosuppressant Effects/Increased Susceptibility to Infections**

Administration of live or live-attenuated vaccines in patients immunocompromised by chemotherapeutic agents including idarubicin may result in serious or fatal infections. Vaccination with a live vaccine should be avoided in patients receiving idarubicin. Killed or inactivated vaccines may be administered; however, the response to such vaccines may be diminished.

#### **Special Populations**

##### **Pregnant Women:**

The embryotoxic potential of idarubicin has been demonstrated in both *in vitro* and *in vivo* studies. However, there are no adequate and well-controlled studies in pregnant women. Therefore, women of childbearing potential should be prescribed effective contraceptive methods and counselled on the risks of pregnancy. Idarubicin should be used during pregnancy only if the potential benefit justifies the potential risk to the

fetus. The patient should be informed of the potential hazard to the fetus if idarubicin hydrochloride injection is to be used during pregnancy, or if the patient becomes pregnant during therapy.

##### **Nursing Women:**

It is not known whether idarubicin or its metabolites are excreted in human milk. Mothers should be advised not to breastfeed while undergoing chemotherapy with idarubicin hydrochloride injection.

##### **Monitoring and Laboratory Tests**

Therapy with idarubicin hydrochloride injection requires close observation of the patient and laboratory monitoring (see **WARNINGS AND PRECAUTIONS, General**).

Cardiac function should be assessed before patients undergo treatment with idarubicin and must be monitored throughout therapy to minimize the risk of incurring severe cardiac impairment (see **WARNINGS AND PRECAUTIONS, Cardiovascular**).

Liver and kidney functions should be evaluated with conventional clinical laboratory tests (using serum bilirubin and serum creatinine as indicators) prior to and during treatment (see **WARNINGS AND PRECAUTIONS, Hepatic/Biliary/Pancreatic** and **WARNINGS AND PRECAUTIONS, Renal**).

Hematologic profiles should be assessed before and during each cycle of therapy with idarubicin including differential white blood cell (WBC) counts (see **WARNINGS AND PRECAUTIONS, Hematologic**).

#### **ADVERSE REACTIONS**

##### **Cardiovascular:**

sinus tachycardia, ECG abnormalities, tachyarrhythmias, atrioventricular and bundle branch block, asymptomatic reductions in LEV, CHF, pericarditis, myocarditis

##### **Hematologic:**

leukopenia, neutropenia, anemia, thrombocytopenia, hemorrhage

##### **Gastrointestinal:**

anorexia, nausea/vomiting, dehydration, mucositis/stomatitis, esophagitis, abdominal pain or burning sensation, erosions/ulceration, gastrointestinal tract bleeding, diarrhea, colitis, including severe enterocolitis/neutropenic enterocolitis with perforation

##### **Liver:**

elevation of liver enzymes and bilirubin

##### **Endocrine:**

hot flashes

##### **Skin:**

alopecia, local toxicity (see **WARNINGS AND PRECAUTIONS**), rash/itch, skin changes, skin and nail hyperpigmentation, hypersensitivity of irradiated skin ('radiation recall reaction'), urticaria, acral erythema

##### **Vascular:**

phlebitis, thrombophlebitis, thromboembolism

##### **Urological:**

red colour to the urine for 1 - 2 days after administration

##### **Other:**

anaphylaxis, infection, sepsis/septicemia, secondary leukemias (acute myeloid leukemia and myelodysplastic syndrome), fever, shock, hyperuricemia

Severe and sometimes fatal infections have been associated with idarubicin alone or in combination with cytarabine. Acute toxicities such as nausea and vomiting, mucositis, diarrhea and liver dysfunction are comparable to those of daunorubicin.

Idarubicin appears to have a cardiac toxicity potential which is similar to that of daunorubicin. Overall, the incidence of serious cardiac events has been 2.0% out of 1204 patients receiving idarubicin via i.v. administration. If patients previously treated with anthracyclines are excluded, the overall incidence is 1.58%. When idarubicin was administered orally, the incidence of serious cardiac events (grade 3 only) was 3.2%.

#### **DRUG INTERACTIONS**

##### **Drug-Drug Interactions**

Idarubicin is a potent myelosuppressant; combination chemotherapy regimens that contain other agents with similar action (e.g., other anthracyclines, anthracenediones) may lead to additive toxicity, especially with regard to bone marrow/hematologic and gastrointestinal effects (see **WARNINGS AND PRECAUTIONS**). Combination chemotherapy regimens that contain other agents, which may potentiate additive hematological toxicity, may include alkylating agents (e.g., cyclophosphamide), antineoplastic agents (such as etoposide, cytarabine, fludarabine), and corticosteroids (e.g., dexamethasone). The use of idarubicin in combination chemotherapy with other potentially cardiotoxic drugs (e.g., cyclophosphamide, paclitaxel), as well as the concomitant use of other cardioactive compounds (e.g., calcium channel blockers such as amlodipine, diltiazem or verapamil), requires monitoring of cardiac function throughout treatment. Changes in hepatic or renal function induced by concomitant therapies may affect idarubicin metabolism, pharmacokinetics, and therapeutic efficacy and/or toxicity.

An additive myelosuppressant effect may occur when radiotherapy is given concomitantly or within 2 - 3 weeks prior to treatment with idarubicin. Interactions with other drugs have not been established.

Precipitation occurs with heparin. Prolonged contact with any solution of an alkaline pH will result in degradation of the drug.

#### **Drug-Food Interactions**

Interactions with food have not been established.

#### **Drug-Herb Interactions**

Interactions with herbal products have not been established.

#### **Drug-Laboratory Interactions**

Interactions with laboratory tests have not been established.

### **DOSSAGE AND ADMINISTRATION**

As with all parenteral products, intravenous solutions should be inspected visually for clarity, particulate matter, precipitate, discoloration and leakage prior to administration. Solutions showing haziness, particulate matter, precipitate, discoloration or leakage should not be used. **Discard unused portions.**

#### **Dosing Considerations**

- These dose schedules should take into account the hematological status of the patient and the dosage of the other cytotoxic drugs when used in combination.
- Hepatic or Renal Dysfunction: While no specific dose recommendation can be made based on the limited available data in patients with hepatic and/or renal impairment, dose reductions should be considered in patients with bilirubin and/or creatinine serum levels greater than 2.0 mg/dL (see **WARNINGS AND PRECAUTIONS**).
- The total dose of Idarubicin Hydrochloride Injection administered to a patient should take into account: prior or concomitant therapy with related compounds such as epirubicin and daunorubicin or anthracene derivatives, and/or radiotherapy to the mediastinal area.

#### **Recommended Dose and Dosage Adjustment**

##### **Acute Non-Lymphocytic Leukemia (ANLL)**

In adults, for remission induction as front-line therapy or for remission induction in relapsed or refractory patients, the following dose schedules are recommended:

- (a) 12 mg/m<sup>2</sup> daily by intravenous injection for 3 days in combination with cytarabine, or
- (b) 8 mg/m<sup>2</sup> daily by intravenous injection as a single agent for 5 days.

##### **Acute Lymphocytic Leukemia (ALL)**

As a second-line treatment, the following dose schedules are recommended:

- (a) in adults, 12 mg/m<sup>2</sup> daily by intravenous injection for 3 days as a single agent, or
- (b) in children, 10 mg/m<sup>2</sup> daily by intravenous injection for 3 days as a single agent.

#### **Administration**

Idarubicin hydrochloride injection **must not** be administered by intramuscular or subcutaneous injection. Unless specific compatibility data are available, idarubicin hydrochloride injection should not be mixed with other drugs. Precipitation occurs with heparin. Prolonged contact with any solution of an alkaline pH will result in degradation of the drug.

Idarubicin hydrochloride injection should be slowly administered into the tubing of a freely running intravenous infusion of Sodium Chloride Injection, USP 0.9%. The tubing should be attached to a Butterfly® needle or other suitable device and inserted preferably into a large vein. If possible, avoid veins over joints or in extremities with compromised venous or lymphatic drainage. The rate of administration is dependent on the size of the vein and the dosage. However, the dosage should be administered over 5 to 10 minutes. Local erythematous streaking along the vein as well as facial flushing may be indicative of too rapid administration. A burning or stinging sensation may be indicative of perivenous infiltration and the infusion should be immediately terminated and restarted in another vein. Perivenous infiltration may occur painlessly. A direct push injection is not recommended due to the risk of extravasation, which may occur even in the presence of adequate blood return upon needle aspiration (see **WARNINGS AND PRECAUTIONS**).

If it is known or suspected that subcutaneous extravasation has occurred, it is recommended that intermittent ice packs (1/2 hour immediately, then 1/2 hour 4 times per day for 3 days) be placed over the area of extravasation and that the affected extremity be elevated. Because of the progressive nature of extravasation reactions, the area of injection should be frequently examined and plastic surgery consultation obtained early if there is any sign of a local reaction such as pain, erythema, edema or vesication. If ulceration begins or there is severe persistent pain at the site of extravasation, early wide excision of the involved area should be considered.

### **OVERDOSAGE**

For management of a suspected drug overdose, contact your regional Poison Control Centre immediately.

Very high doses of idarubicin hydrochloride injection may be expected to cause acute myocardial toxicity within 24 hours and severe myelosuppression within 1 or 2 weeks.

Treatment should aim to support the patient during this period and should utilize such measures as blood transfusions and reverse-barrier nursing. Delayed cardiac failure has been seen with the anthracyclines up to several months after the overdose. Patients should be observed carefully and, if signs of cardiac failure arise, should be treated along conventional lines.

### **ACTION AND CLINICAL PHARMACOLOGY**

#### **Mechanism of Action**

Idarubicin, either as a single agent or in combination, has been shown to be a potent antileukemic agent capable of inducing complete remission in previously untreated and in relapsed and refractory acute non-lymphocytic leukemia (ANLL) including resistant patients, and in adult and pediatric relapsed patients with acute lymphoblastic leukemia (ALL).

Idarubicin is a DNA-intercalating analog of daunorubicin which has an inhibitory effect on nucleic acid synthesis and interacts with the enzyme topoisomerase II. The modification, in position 4 of the anthracycline structure, gives the compound a high lipophilicity which results in an increased rate of cellular uptake compared with other anthracyclines.

Idarubicin has been shown to have a higher potency than daunorubicin and to be an effective agent against murine leukemias and lymphomas. *In vitro* studies on human and murine anthracycline-resistant cells have revealed a lower degree of cross resistance for idarubicin in comparison with doxorubicin and daunorubicin.

#### **Pharmacokinetics**

Seven pharmacokinetic studies were carried out in 49 patients. The plasma concentrations of idarubicin fit a 2 or 3 compartment open models.

Studies of cellular (nucleated blood and bone marrow cells) drug concentrations in leukemic patients have shown that peak cellular idarubicin concentrations are reached a few minutes after injection. Idarubicin and idarubicinol concentrations in nucleated blood and bone marrow cells are more than 100 times the plasma concentrations. Idarubicin disappearance rates in plasma and cells were comparable with a terminal half-life of about 15 hours. The terminal half-life of idarubicinol in cells was about 72 hours.

#### **Absorption:**

After oral administration to patients with normal renal and hepatic function, idarubicin is rapidly absorbed, with a peak time of 2 - 4 hours.

#### **Distribution:**

The absolute bioavailability of idarubicin given orally has been shown to range between 18 and 39%, whereas that calculated from the data on the active metabolite, idarubicinol, is somewhat higher (29 - 58%). The effective bioavailability, calculated on the basis of the pharmacological response, is approximately 35%. Protein binding was studied *in vitro* by equilibrium dialysis at concentrations of idarubicin and idarubicinol similar to the maximum plasma level obtained in the pharmacokinetic studies. The percent of idarubicin and idarubicinol bound to human plasma proteins at the concentration of 100 ng/mL plasma is on the average 97% and 94%, respectively.

#### **Metabolism:**

After intravenous administration to patient with normal renal and hepatic function, idarubicin is extensively metabolized to an active metabolite, idarubicinol.

#### **Excretion:**

After intravenous administration to patients with normal renal and hepatic function, idarubicin is eliminated from systemic circulation with a terminal plasma half-life ranging between 11 - 25 hours. Active metabolite, idarubicinol, is more slowly eliminated with a plasma half-life ranging between 41 - 69 hours. The drug is eliminated by biliary and renal excretion, mostly in the form of active metabolite idarubicinol.

After oral administration to patients with normal renal and hepatic function, idarubicin is rapidly absorbed, with a peak time of 2 - 4 hours. It is rapidly eliminated from systemic circulation with a terminal plasma  $t_{1/2}$  ranging between 10 - 35 hours and is extensively metabolized to an active metabolite, idarubicinol. Idarubicinol is more slowly eliminated with a plasma  $t_{1/2}$  ranging between 33 - 60 hours.

### **STORAGE AND STABILITY**

Idarubicin Hydrochloride Injection should be stored between 2 and 8°C and protected from light.

#### **Incompatibility**

Unless specific compatibility data are available, Idarubicin Hydrochloride Injection should not be mixed with other drugs. Precipitation occurs with heparin. Prolonged contact with any solution of an alkaline pH will result in degradation of the drug.

### **SPECIAL HANDLING INSTRUCTIONS**

#### **Preparation and handling**

1. Personnel should be trained in good techniques for handling.

Pregnant staff should be excluded from working with this drug.

2. Preparation of antineoplastic solutions should be done in a vertical laminar flow hood (Biological Safety Cabinet - Class II). The work surface should be protected by disposable, plastic-backed, absorbent paper.
3. Personnel preparing idarubicin solutions should wear PVC gloves, safety glasses and protective clothing such as disposable gowns and masks. If idarubicin contacts the skin or mucosa, the area should be washed with soap and water immediately.
4. Personnel regularly involved in the preparation and handling of antineoplastics should have blood examinations on a regular basis.

#### **Disposal**

1. Avoid contact with skin and inhalation of airborne particles by use of PVC gloves and disposable gowns and masks.
2. All needles, syringes, vials and other materials which have come in contact with idarubicin hydrochloride injection should be segregated in plastic bags, sealed and marked as hazardous waste. Incinerate at 1000°C or higher. Sealed containers may explode if a tight seal exists.
3. If incineration is not available, idarubicin hydrochloride injection may be detoxified by adding sodium hypochlorite solution (household bleach) to the vial, in sufficient quantity to decolorize the idarubicin, care being taken to vent the vial to avoid a pressure build-up of the chlorine gas which is generated. Dispose detoxified vials in a safe manner.

#### **Needles, syringes, disposable and non-disposable equipment**

Rinse equipment with an appropriate quantity of sodium hypochlorite solution. Discard the solution in the sewer system with running water and discard disposable equipment in a safe manner. Thoroughly wash non-disposable equipment in soap and water.

#### **Spillage/Contamination**

Wear gloves, mask, protective clothing. Treat spilled powder or liquid with dilute sodium hypochlorite (1% available chlorine) solution. Carefully absorb solution with gauze or towels again and place in polyethylene bag; seal, double bag and mark as hazardous waste. Dispose waste by incineration or by other methods approved for hazardous materials. Personnel involved in cleanup should wash with soap and water.

#### **DOSAGE FORMS, COMPOSITION AND PACKAGING**

Each mL of solution contains idarubicin hydrochloride, USP 1 mg and the following inactive ingredients: glycerin, USP 25 mg and Water for Injection, USP q.s., hydrochloric acid, NF is used to adjust the pH to a target of 3.5.

Idarubicin Hydrochloride Injection is available in the following form and package sizes:

- C109405 **Idarubicin Hydrochloride Injection:** 5 mg/5 mL vial (1 mg/mL) in a single-dose vial individually packaged
- C109410 **Idarubicin Hydrochloride Injection:** 10 mg/10 mL vial (1 mg/mL) in a single-dose vial individually packaged
- C109420 **Idarubicin Hydrochloride Injection:** 20 mg/20 mL vial (1 mg/mL) in a single-dose vial individually packaged

Vial stoppers do not contain natural rubber latex.