Idarubicin hydrochloride for Injection U.S.P.

ZAVEDOS®

1. GENERIC NAME

Idarubicin hydrochloride

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Idarubicin hydrochloride is available as:

Freeze dried powder for solution for injection containing idarubicin hydrochloride U.S.P. 5 mg

List of excipients

Freeze dried powder for solution for injection:
Lactose (as lactose anhydrous)

3. DOSAGE FORM AND STRENGTH

Freeze dried powder for solution for injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Intravenous Administration

Antimitotic and cytotoxic agent.

Adults

Acute myeloid leukemia (AML): for the induction of the remission both as first line therapy and for remission induction in relapsed or refractory patients.

Acute lymphocytic leukemia (ALL): second-line treatment.

®Trademark Proprietor: Pfizer Italia S.r.L.
Licensed user: Pfizer Products India Private Limited, India

Children

Acute lymphocytic leukaemia (ALL): second line therapy.

4.2 Posology and method of administration

Intravenous Administration

Idarubicin, either as the reconstituted solution or the ready to use solution must be administered only by the intravenous (IV) route (See section **8.4**). A slow administration over 5 to 10 minutes via the tubing of a freely running intravenous infusion of 0.9% sodium chloride or 5% dextrose must be followed. 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 section **4.4**).

- **AML**
  Adult
  The recommended intravenous dose schedule is 12 mg/m^2 daily for 3 days in combination with cytarabine. Idarubicin may also be administered as a single agent and in combination, at a dose of 8 mg/m^2 daily for 5 days.

  NOTE: These are general guidelines. Refer to individual protocols for exact dosage.

- **ALL**
  Adult
  The recommended single-agent intravenous dose is 12 mg/m^2 daily for 3 days.

  Children
  The recommended single-agent intravenous dose is 10 mg/m^2 daily for 3 days.

  NOTE: These are general guidelines. Refer to individual protocols for exact dosage.

Dose Modifications

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 % (See section **4.4**).

Idarubicin should not be administered to patients with severe hepatic and/or renal impairment (See section **4.3**).

4.3 Contraindications

- Hypersensitivity to idarubicin or any other component of the product, listed in section **2**, other anthracyclines or anthracenediones
- Severe hepatic impairment

- Severe renal impairment
- Severe cardiomyopathy
- Recent myocardial infarction
- Severe arrhythmias
- Persistent myelosuppression
- Previous treatment with maximum cumulative doses of idarubicin and/or other anthracyclines and anthracenediones (See section **4.4**)
- Breast-feeding should be stopped during drug therapy (See section **4.6**)
- Pregnant women or women wishing to become pregnant

4.4 Special warnings and precautions for use

General: Idarubicin should be administered only under the supervision of physicians experienced in the use of cytotoxic chemotherapy. Close monitoring for toxicity is mandatory. The drug should not be given to patients with pre-existing bone marrow depression induced by previous drug therapy or radiotherapy unless the benefit warrants the risk.

This ensures that immediate and effective treatment of severe complications of the disease and/or its treatment (e.g. hemorrhage, overwhelming infections) may be carried out.

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

Cardiac Function: 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 electrocardiogram (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 reason for the discontinuation of idarubicin treatment.

Late (i.e., Delayed) Events: Delayed cardiotoxicity usually develops late in the course of therapy or within 2 to 3 months after treatment termination, 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, 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 IV or oral idarubicin have not been defined. However, idarubicin-related cardiomyopathy was reported in 5% of patients who received cumulative IV

doses of 150 to 290 mg/m^2. Available data on patients treated with oral idarubicin total cumulative doses up to 400 mg/m^2 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 Multiple Gated Acquisition (MUGA) scan 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 (e.g., trastuzumab). Anthracyclines including idarubicin should not be administered in combination with other cardiotoxic agents unless the patient's cardiac function is closely monitored (See section **4.5**). 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 reported half-life of trastuzumab is approximately 28-38 days and may persist in the circulation for up to 27 weeks. Therefore, physicians should avoid anthracycline-based therapy for up to 27 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 occur at lower cumulative doses whether or not cardiac risk factors are present.

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 has to be performed.

It is probable that the toxicity of idarubicin and other anthracyclines or anthracenediones is additive.

Hematologic Toxicity: Idarubicin is a potent bone marrow suppressant. Severe myelosuppression will 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 after drug administration; however, cell counts generally return to normal levels during the third week. Clinical consequences of severe myelosuppression include fever,

infections, sepsis/septicemia, septic shock, hemorrhage, tissue hypoxia, or death. If febrile neutropenia occurs, treatment with an IV antibiotic is recommended.

Secondary Leukemia: 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, when patients have been heavily pretreated with cytotoxic drugs, or when doses of the anthracyclines have been escalated. These leukemias can have a 1- to 3-year latency period.

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 a severe haemorrhagic condition and/or severe infection rapidly and effectively.

Gastrointestinal: Idarubicin is emetigenic. 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. The risk of perforation may be increased by instrumental intervention. The possibility of perforation should be considered in patients who develop severe abdominal pain and appropriate steps for diagnosis and management should be taken.

Hepatic and/or Renal Function: Since hepatic and/or renal function impairment can affect the disposition of idarubicin, liver and kidney function should be evaluated with conventional clinical laboratory tests (using serum bilirubin and serum creatinine as indicators) prior to, and during, treatment. In a number of Phase III clinical trials, treatment was contraindicated if bilirubin and/or creatinine serum levels exceeded 2.0-mg %. With other anthracyclines a 50% dose reduction is generally used if bilirubin levels are in the range 1.2 to 2.0-mg % (See section **4.2**).

Effects at Site of Injection: Phlebosclerosis may result from an injection into a small vessel or from previous injections into the same vein. Following the recommended administration procedures may minimize the risk of phlebitis/thrombophlebitis at the injection site (See section **4.2**).

Extravasation: Extravasation of idarubicin during intravenous injection may cause local pain, severe tissue lesions (vesication, severe cellulitis), and necrosis. Should signs or symptoms of extravasation occur during intravenous administration of idarubicin, the drug infusion should be immediately stopped. In cases of extravasation, dexrazoxane can be used to prevent or reduce tissue injury.

Tumor Lysis Syndrome: Idarubicin may induce hyperuricemia as a consequence of the extensive purine catabolism that accompanies rapid drug-induced 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.

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.

Reproductive System: Men treated with idarubicin hydrochloride are advised to adopt contraceptive measures during therapy and up to 6 months afterwards and, if appropriate and available, to seek advice on sperm preservation due to the possibility of irreversible infertility caused by the therapy (see paragraph **4.6**).

Other: As with other cytotoxic agents, thrombophlebitis and thromboembolic phenomena, including pulmonary embolism have been coincidentally reported with the use of idarubicin. Patients should be advised that the product can cause red coloration of the urine for 1-2 days after administration.

Important Information About Some of the Ingredients
Idarubicin hydrochloride 5 mg/5 mL powder and solvent for solution for injection for intravenous use contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp-lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Drugs Interactions

Idarubicin is a potent myelosuppressant and combination chemotherapy regimens that contain other agents with similar action may lead to additive toxicity, especially with regard to bone marrow/hematologic and gastrointestinal effects (See section **4.4**). The use of idarubicin in combination chemotherapy with other potentially cardiotoxic drugs, as well as the concomitant use of other cardioactive compounds (e.g., calcium channel blockers), 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 (See section **4.4**).

An additive myelosuppressant effect may occur when radiotherapy is given concomitantly or within 2-3 weeks prior to treatment with idarubicin.

Concomitant use not recommended.

Live-attenuated vaccines (except yellow fever, which is contraindicated): Risk of possibly fatal systemic disease. This risk is increased in subjects who are already immunosuppressed by their underlying disease.

Use an inactivated vaccine where this exists (poliomyelitis).

At combination of oral anticoagulants and anticancer chemotherapy, increased frequency of the INR (International Normalised Ratio) monitoring is recommended, since the risk for an interaction cannot be excluded.

Cyclosporin A: The co-administration of cyclosporin A as a single chemosensitizer significantly increased idarubicin AUC (1.78-fold) and idarubicinol AUC (2.46-fold) in patients with acute leukemia. The clinical significance of this interaction is unknown.

A dosage adjustment may be necessary in some patients.

4.6 Use in special populations

Impairment of Fertility: Idarubicin can induce chromosomal damage in human spermatozoa. For this reason, males undergoing treatment with idarubicin should use effective contraceptive methods up to 3 months after treatment (See section **4.4**).

Pregnancy: 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. Women of child-bearing potential should be advised to avoid becoming pregnant during treatment. 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.

Patients desiring to have children after completion of therapy should be advised to obtain genetic counselling first if appropriate and available.

Lactation: It is not known whether idarubicin or its metabolites are excreted in human milk. Mothers should be advised not to breast-feed while undergoing chemotherapy with this drug.

4.7 Effects on ability to drive and use machines

The effect of idarubicin on the ability to drive or use machinery has not been systematically evaluated. Special care should be taken if it is essential that patients drive or operate machinery while undergoing treatment with idarubicin, especially if in a debilitated condition.

4.8 Undesirable effects

The frequencies of undesirable effects are based on the following categories:

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not known (cannot be estimated from the available data)

Infections and infestations	
Very common	Infections

Uncommon	Sepsis, septicemia
Neoplasms benign, malignant and unspecified (including cysts and polyps)	
Uncommon	Secondary leukemia (acute myeloid leukemia and myelodysplastic syndrome)
Blood and lymphatic system disorders	
Very common	Anemia, leukopenia, neutropenia, thrombocytopenia
Not Known	Pancytopenia
Immune system disorders	
Very rare	Anaphylaxis
Endocrine disorders	
Very common	Anorexia
Uncommon	Dehydration
Metabolism and nutrition disorders	
Uncommon	Hyperuricemia
Not Known	Tumour Lysis Syndrome
Nervous system disorders	
Rare	Cerebral hemorrhages
Cardiac disorders	
Common	Congestive heart failure, sinus tachycardia, tachyarrhythmia, asymptomatic reduction of left ventricular ejection fraction, bradycardia, cardiomyopathies (See section **4.4** for associated signs and symptoms)
Uncommon	ECG abnormalities (e.g. nonspecific ST segment changes), myocardial infarction
Very rare	Pericarditis, myocarditis, atrioventricular and bundle branch block
Vascular disorders	
Common	Haemorrhages, local phlebitis, thrombophlebitis
Uncommon	Shock

Very rare	Thromboembolism, flush
Gastrointestinal disorders	
Very common	Nausea, vomiting, mucositis/stomatitis, diarrhea, abdominal pain or burning sensation
Common	Gastrointestinal tract bleeding, bellyache
Uncommon	Esophagitis, colitis (including severe enterocolitis/neutropenic enterocolitis with perforation)
Very rare	Gastric erosions or ulcerations
Hepatobiliary disorders	
Common	Elevation of the liver enzymes and bilirubin
Skin and subcutaneous tissue disorders	
Very common	Alopecia
Common	Rash, Itch, hypersensitivity of irradiated skin ('radiation recall reaction')
Uncommon	Skin and nail hyperpigmentation, urticaria, cellulites (This event can be severe), tissue necrosis
Very rare	Acral erythema
Unknown	Local reaction
Renal and urinary disorders	
Very common	Red coloration of the urine for 1 – 2 days after the treatment.
General disorders and administration site conditions	
Very common	Fever, headache, chills
Common	Hemorrhages
Uncommon	Dehydration

Description of selected adverse reactions

Hematopoietic system
Pronounced myelosuppression is the most serious side effect. However, this is necessary for the eradication of leukemic cells (See section **4.4**).

Gastrointestinal
Stomatitis and in severe cases ulceration of mucosa, dehydration caused by severe vomiting and diarrhoea; risk of perforation of colon etc.

Administration site
Phlebitis/thrombophlebitis and prevention measures discussed in section **4.2**; paravenous unintended infiltrates may cause pain, severe cellulites and tissue necrosis.

Other adverse reactions:

Hyperuricaemia
Prevention of symptoms by hydration, urine alkalinisation, and prophylaxis with allopurinol may minimise potential complications of tumor lysis syndrome.

Cardiotoxicity
Life-threatening CHF is the most severe form of anthracycline-induced cardiomyopathy and represents the cumulative dose-limiting toxicity of the drug (See section **4.4**).

Endocrine
Vasomotor instability (hot flushes) have been reported.

Paediatric population
Undesirable effects are similar in adults and children except a greater susceptibility to anthracycline-induced cardiac toxicity of children (see section **4.4**).

4.9 Overdose

Very high doses of idarubicin may cause acute myocardial toxicity within 24 hours and severe myelosuppression within 1 to 2 weeks. Delayed cardiac failure has been seen with the anthracyclines up to several months after the overdose.

Patients treated with oral idarubicin should be observed for possible gastrointestinal hemorrhage and severe mucosal damage.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of action

Pharmaco-therapeutic Group: cytotoxic antibiotics – anthracyclines.
ATC Code: L01DB06

Idarubicin is a DNA intercalating analogue of daunorubicin, which has an inhibitory effect on nucleic acid synthesis and interacts with the enzyme topoisomerase II. The absence of a methoxy group at position 4 of the anthracycline structure gives the compound a high lipophilicity, which results in an increased rate of cellular uptake compared with doxorubicin and daunorubicin.

5.2 Pharmacodynamic properties

Idarubicin has been shown to have a higher potency with respect to daunorubicin and to be an effective agent against murine leukemia and lymphomas both by IV and oral routes. Studies

in vitro on human and murine anthracycline-resistant cells have shown a lower degree of cross-resistance for idarubicin compared with doxorubicin and daunorubicin. Cardiotoxicity studies in animals have indicated that idarubicin has a better therapeutic index than daunorubicin and doxorubicin. The main metabolite, idarubicinol, has shown, *in vitro* and *in vivo,* antitumoral activity in experimental models. In the rat, idarubicinol, administered at the same doses as the parent drug, is clearly less cardiotoxic than idarubicin.

5.3 Pharmacokinetic properties

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

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 a hundred times the plasma concentrations. Idarubicin disappearance rates in plasma and cells were almost comparable with a terminal half-life of about 15 hours. The terminal half-life of idarubicinol in cells was about 72 hours.

Special populations
Hepatic and renal impairment: The pharmacokinetics of idarubicin in patients with hepatic and/or renal impairment have not been fully evaluated. It is expected that in patients with moderate or severe hepatic dysfunction, the metabolism of idarubicin may be impaired and lead to higher systemic drug levels. The disposition of idarubicin may also be affected by renal impairment. Therefore, a dose reduction should be considered in patients with hepatic and/or renal impairment (See sections **4.2** and **4.4**) and idarubicin is contraindicated in patients with severe hepatic and/or renal failure (See section **4.3**).

Paediatric population
Pharmacokinetic measurements in 7 paediatric patients receiving intravenous idarubicin in doses ranging from 15 to 40 mg/m^2 for 3 days of treatment, showed a median idarubicin half-life of 8.5 hrs (range: 3.6-26.4 hrs). The active metabolite, idarubicinol, accumulated during the 3 days of treatment, exhibiting a median half-life of 43.7 hrs (range: 27.8-131 hrs).

Total body clearance values of 30-107.9 L/h/m^2 for idarubicin reported for adults are higher than the values of 18-33 L/h/m^2 reported for paediatric populations. Although idarubicin has a very large volume of distribution in both adults and children, suggesting that much of the drug is bound to tissues, the shorter elimination half-life and lower total body clearance are not entirely explained by a smaller apparent volume of distribution in children compared to adults.

6. NONCLINICAL PARTICULARS

6.1 Animal toxicology or pharmacology

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. No noteworthy effects on the mothers or offspring were seen in rats given intravenous idarubicin during the peri- and post-natal periods up to the dose of 0.2 mg/kg/day. It is not known whether the compound is excreted in breast milk. Intravenous idarubicin, like other anthracyclines and cytotoxic drugs, was carcinogenic in rats. A local safety study in dogs showed that extravasation of the drug causes tissue necrosis.

The LD_{50} (mean values) of intravenous idarubicin was 4.4 mg/kg for mice, 2.9 mg/kg for rats and about 1.0 mg/kg for dogs. The main targets after a single dose were the hemolymphopoietic system and, especially in dogs, the gastrointestinal tract.

The toxic effects after repeated administration of intravenous idarubicin were investigated in rats and dogs. The main targets of intravenous idarubicin in the above animal species were the hemolymphopoietic system, gastrointestinal tract, kidney, liver, and male and female reproductive organs.

Concerning the heart, subacute and cardiotoxicity studies indicated that intravenous idarubicin was slightly to moderately cardiotoxic only at lethal doses while doxorubicin and daunorubicin produced clear myocardial damage at non-lethal doses.

7. DESCRIPTION

Colourless glass vials containing a porous, redorange freeze-dried cake or mass

8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

Idarubicin should not be mixed with other drugs. Contact with any solution of an alkaline pH should be avoided as it will result in degradation of the drug. Idarubicin should not be mixed with heparin due to chemical incompatibility that may lead to precipitation.

8.2 Shelf-life

36 months

8.3 Packaging information

Freeze dried powder for solution for injection: Glass vial

8.4 Storage and handling instructions

Freeze dried powder for solution for injection:
Store below 30°C. Keep out of the reach of children.

The reconstituted solution is chemically stable when stored for atleast 48 hours at 2°C-8°C and 24 hours at temperature upto 25°C; however it is recommended that, in line with good pharmaceutical practice the solution should not normally be stored for longer than 24 hours at 2°C-8°C.

Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Freeze dried powder for solution for injection:
The vial contents are under negative pressure to minimize aerosol formation during reconstitution: particular care should be taken when the needle is inserted. Inhalation of any aerosol produced during reconstitution must be avoided.

The following protective recommendations which are valid for all cytotoxic agents are given:

- personnel should be trained in good technique for reconstitution and handling;
- pregnant staff should be excluded from working with this drug;
- personnel handling the drug should wear protective clothing: goggles, gowns and disposable gloves and masks;
- a designated area should be defined for reconstitution (preferably under a vertical laminar flow system). The work surface should be disposable, plastic-backed, absorbent paper;
- all items used for reconstitution, administration or cleaning, including gloves, should be placed in high-risk waste disposal bags for high temperature incineration.
- Accidental contact with the skin or eyes should be treated immediately by copious lavage with water: medical attention should be sought.
- Spillage or leakage should be treated with dilute sodium hypochlorite (1% available chlorine) solution, preferably by soaking, and then water. All cleaning materials should subsequently be disposed of as indicated previously.

Discard any unused solution.

Prolonged contact with any solution of an alkaline pH should be avoided as it will result in degradation of the drug.

Idarubicin hydrochloride should not be mixed with heparin as a precipitate may form and it is not recommended that it is mixed with other drugs.

9. DETAILS OF MANUFACTURER

MANUFACTURED BY :
M/s. Actavis Italy S.p.A. Viale Pasteur 10 Nerviano MI - 20014 NA (Italy).

IMPORTED AND MARKETED IN INDIA BY :
Pfizer Products India Private Limited, The Capital- B Wing, 1802, 18th Floor, Plot No. C-70, G-Block, Bandra Kurla Complex, Bandra (East), Mumbai 400 051, India.

10. DETAILS OF PERMISSION OR LICENSE NUMBER WITH DATE

FF-579-19222 dated 04-Jun-2020* (*The license is renewed every 3 years as per regulations).

11. DATE OF REVISION

July 2020