SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Idarubicin 20 mg/20 ml solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial of 20 ml contains 20 mg of idarubicin hydrochloride.

Each ml of solution contains 1 mg idarubicin hydrochloride.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

Clear, orange red solution, free of visible suspended particles.

pH: 3 - 4.5

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Cytotoxic and antimitotic agent.

Adults

- For the treatment of acute myeloid leukaemia (AML), for remission induction in untreated patients or for remission induction in relapsed or refractory patients.

- For second line treatment of relapsed acute lymphoblastic leukaemia (ALL).

Children

- For first line treatment of acute myeloid leukaemia (AML), in combination with cytarabine, for remission induction.

- For second line treatment of relapsed acute lymphoblastic leukaemia (ALL).

Idarubicin Accord may be used in combination chemotherapy regimens involving other cytotoxic agents (see section 4.2).

4.2 Posology and method of administration

Posology
Dosage is usually calculated on the basis of body surface area (mg/m^2). For intravenous use.

Acute non-lymphocytic leukaemia (AML)

Adults: In acute non-lymphocytic leukaemia the recommended dose is 12 mg/m^2 IV daily for 3 days in combination with cytarabine. Other dose schedule which could be used in acute non-lymphocytic leukaemia, as a single agent or in combination, is 8 mg/m^2 IV daily for 5 days.
Children: the recommended dose range is 10-12 mg/m^2 i.v. daily for 3 days in combination with cytarabine.

Acute lymphocytic leukaemia (ALL)

Adults: As single agent the suggested dose is 12 mg/m^2 i.v. daily for 3 days.

Children: As single agent the suggested dose is 10 mg/m^2 i.v. daily for 3 days

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

All of the dosage schedules should take into account the haematological status of the patient, and the dosages of other cytotoxic drugs when used in combination.

Method of administration
Intravenous administration of idarubicin should be performed carefully. It's recommended that idarubicin is given via the tubing of a freely running intravenous infusion of 0.9% sodium chloride injection taking 5 to 10 minutes over the injection. This technique minimises the risk of thrombosis or perivenous extravasation which can lead to severe cellulitis, vesication and tissue necrosis. Direct injection is not recommended, due to the risk of extravasation, which may occur even with the adequate blood return by aspiration through the needle.

4.3 Contraindications

- Hypersensitivity to idarubicin or to any of the excipients listed in section 6.1
- Hypersensitivity to other anthracyclines or anthracenediones
- Severe hepatic impairment
- Severe renal impairment

- Uncontrolled infections
- 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)
- Breastfeeding should be stopped during drug therapy (see section 4.6)

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. Therapy with Idarubicin requires close observation of patient and laboratory monitoring. This ensures that immediate and effective treatment of severe complications of the disease and/or its treatment (e.g. hemorrhage, overhelming infections) may be carried out.

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

Cardiac function
Cardiotoxicity is a known risk of treatment with anthracyclines that may manifest itself as early (i.e. acute) or late (i.e. delayed) events.

Early (acute) events: Early cardiotoxicity of idarubicin consists mainly of sinus tachycardia and/or electrocardiogram (ECG) abnormalities, such as non-specific ST-T wave changes. Tachyarrhythmia, including premature ventricular contractions and ventricular tachycardia, bradycardia as well as atrioventricular and bundle branch block have also been reported. These effects are not usually predictors of subsequent development of delayed cardiotoxicity, are rarely of clinical importance and are generally not a reason for discontinuation of Idarubicin treatment.

Late (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 dyspnoea, pulmonary oedema, dependent oedema, cardiomegaly, hepatomegaly, oliguria, ascites, pleural effusion and gallop rhythm. Subacute effects such as pericarditis/myocarditis have also been reported. Life-threatening congestive heart failure is the most severe form of anthracycline-induced cardiomyopathy and represents the cumulative dose-limiting toxicity of the drug.

The cumulative dose limits for IV or oral idarubicin hydrochloride 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. The available data on patients treated with oral idarubicin hydrochloride total cumulative doses of 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 minimise 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 consisting of 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 doses of anthracyclines. 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 anthracenedione agents, and concomitant use of drugs capable of suppressing cardiac contractility or cardiotoxic drugs (for example 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 variable. The substance may persist in circulation for up to 7 months. Therefore, physicians should avoid anthracycline-based therapy for up to 7 months after stopping trastuzumab when possible. If this is not possible the patient’s cardiac function should be monitored carefully.

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

Haematological toxicity
Idarubicin is a potent bone marrow suppressant. Severe myelosuppression will occur in all patients given a therapeutic dose of this drug.

Haematological profiles should be assessed before and during each cycle of therapy with idarubicin, including a differential white blood cell (WBC) counts.

A dose-dependent reversible leukopenia and/or granulocytopenia (neutropenia) is the predominant manifestation of idarubicin haematologic toxicity and is the most common acute dose-limiting toxicity of this drug.

Leukopenia and neutropenia are usually severe; thrombocytopenia and anaemia 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. During the phase of severe myelosuppression, deaths due to infections and/or haemorrhages have been reported.

Clinical consequences of severe myelosuppression include fever, infections, sepsis/septicaemia, septic shock, haemorrhage, tissue hypoxia or death. If febrile neutropenia occurs, treatment with an IV antibiotic is recommended.

Secondary leukaemia
Secondary leukaemia, with or without a preleukaemic phase, has been reported in patients treated with anthracyclines, including idarubicin. Secondary leukaemia 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. These leukaemias can have a 1- to 3-years latency period.

Gastrointestinal
Idarubicin is emetigenic. Mucositis (mainly stomatitis, less often oesophagitis) 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 leukaemia 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.

Hepatic and 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/dl. With other anthracyclines a 50% dose reduction is generally used if bilirubin levels are in the range 1.2 - 2.0-mg/dl.

Effects at the injection site
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.

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.

Tumour lysis syndrome
Idarubicin may induce hyperuricemia as a consequence of the extensive purine catabolism that accompanies rapid drug-induced lysis of the neoplastic cells (‘tumour lysis syndrome’). Blood uric acid levels, potassium, calcium, phosphate, and creatinine should be evaluated after initial treatment. Hydration, urine alkalinisation, and prophylaxis with allopurinol to prevent hyperuricemia may minimise potential complications of tumour lysis syndrome.

Immunosuppressive effects/Increased susceptibility to infections
Administration of live or live-attenuated vaccines (like yellow fever) in patients with 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 can be administered; however, the response to such vaccines may be diminished.

Reproductive system
Idarubicin can cause genotoxicity. Male and female patients treated with idarubicin hydrochloride are advised to adopt effective contraceptive measures during therapy and for a period after treatment.
Males treated with idarubicin hydrochloride are advised, if appropriate and available, to seek advice on sperm preservation due to the possibility of irreversible infertility caused by the therapy (see section 4.6). Patients desiring to have children after completion of therapy should be advised to discuss with an appropriate specialist first.

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

This product may cause a red colouration of the urine for 1 - 2 days after administration and patients should be advised of this fact.

Sodium
This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Idarubicin is a potent myelosuppressant and so combination chemotherapy regimens including other agents with similar action may be expected to induce additive myelosuppressive 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 myelosuppressive effect may occur when radiotherapy is given concomitantly or within 2-3 weeks prior to treatment with idarubicin.

Concomitant use of live attenuated vaccines (e.g. yellow fever) is not recommended, due to risk of possibly fatal systemic disease. This risk is increased in subjects who are already immunosuppressed by their underlying disease.

An inactivated vaccine should be used if available.

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 leukaemia. The clinical significance of this interaction is unknown.

A dose adjustment may be necessary in some patients.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is a limited amount of data from the use of idarubicin in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3).

Idarubicin should not be used during pregnancy unless the potential benefit justifies the potential risk to the foetus. The patient should be informed of the potential hazard to the foetus.

Women of childbearing potential/ Contraception in males and females
Women of childbearing potential should be advised not to become pregnant and to use effective contraception during treatment with idarubicin and for at least 6.5 months after the last dose. Men with female partners of childbearing potential should be advised to use effective contraception during treatment with idarubicin and for at least 3.5 months after the last dose (see section 4.4).

Breast-feeding
It is not known whether idarubicin or its metabolites are excreted in human milk. As other anthracyclines are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from idarubicin, women should be advised not to breast-feed during treatment with idarubicin and for at least 14 days after the last dose.

Fertility
Idarubicin can induce chromosomal damage in human spermatozoa. For this reason, males undergoing treatment with idarubicin should use effective contraceptive methods for at least 3.5 months after the last dose (see section 4.4). Both men and women should seek advice on fertility preservation before treatment.

4.7 Effects on ability to drive and use machines

The effect of idarubicin on the ability to drive and use machinery has not been systematically evaluated.

4.8 Undesirable effects

List of adverse reactions

The frequencies of adverse events are ranked according to the following convention: Very common (≥ 1/10); common (≥ 1/100to <1/10); uncommon (≥ 1/1,000to < 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, septicaemia

Neoplasms benign, malignant and unspecified (including cysts and polyps)
Uncommon: Secondary leukemias (acute myeloid leukemia and myelodysplastic syndrome)

Blood and lymphatic system disorders
Very common: Anaemia, severe leukopenia and neutropenia, thrombocytopenia
Not known: Pancytopenia

Immune system disorders
Very rare: Anaphylaxis

Endocrine disorders
Very common: Anorexia
Uncommon: Dehydration

Metabolism and nutrition disorders
Uncommon: Hyperuricaemia
Not known: Tumor lysis syndrome

Nervous system disorders
Rare: Cerebral haemorrhages

Cardiac disorders
Common: Bradycardia, sinus tachycardia, tachyarrhythmia, asymptomatic reductions in left ventricular ejection fraction, congestive heart failure, cardiomyopathies (see section 4.4 in relation to associated signs and symptoms)
Uncommon: ECG abnormalities (e.g., non-specific 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, diarrhoea, abdominal pain or burning sensation
Common: Gastrointestinal tract bleeding, bellyache
Uncommon: Oesophagitis, colitis (including severe enterocolitis/neutropenic enterocolitis with perforation)
Very rare: Gastric erosions or ulcerations

Hepatobiliary disorders
Common: Elevation of 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, cellulitis (possibly severe), tissue necrosis
Very rare: Acral erythema
Not known: Local reaction

Renal and urinary disorders
Very common: Red colour to the urine for 1-2 days after treatment

General disorders and administration site conditions
Very common: Fever, headaches, chills

Description of selected adverse reactions

Haematopoietic system
Pronounced myelosuppression is the most severe adverse effect of idarubicin treatment. However, this is necessary for the eradication of leukemic cells (see section 4.4).

Cardiotoxicity
Life-threatening congestive heart failure is the most severe form of anthracycline-induced cardiomyopathy and represents the cumulative dose-limiting toxicity of the drug (see section 4.4).

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

Administration site
Phlebitis/thrombophlebitis and prevention measures discussed in section 4.2 of SPC; unintended paravenous 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 tumour lysis syndrome.

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).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Very high doses of idarubicin may be expected to cause acute myocardial toxicity within 24 hours and severe myelosuppression within one to two 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 haemorrhage and severe mucosal damage.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Cytotoxic antibiotics; Anthracyclines and related substances

ATC code: L01DB06

Idarubicin is a DNA-intercalating anthracycline which interacts with the enzyme topoisomerase II and has an inhibitory effect on nucleic acid synthesis. The modification of 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. Idarubicin has been shown to have greater potency with respect to daunorubicin and to be an effective agent against murine leukaemia and lymphomas both by i.v. 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,* antitumoural activity in experimental models. In the rat, idarubicinol administered at the same doses as the parent drug, is clearly less cardiotoxic than idarubicin.

5.2 Pharmacokinetic properties

In adults, following oral administration of 10 to 60 mg/m^2 idarubicin, idarubicin was rapidly absorbed with the maximum plasma concentrations of 4-12.65 ng/ml achieved in 1 to 4 hours after dosing. The terminal half-life was 12.7±6.0 hours (mean±SD). Following intravenous administration of idarubicin in adults, the terminal half-life was 13.9±5.9 hours, similar to that observed after the oral administration.

After i.v. administration, idarubicin is extensively metabolised to an active metabolite, idarubicinol, which is slowly eliminated with a plasma $T_{½}$ ranging between 41 – 69 hours. The drug is eliminated by biliary and renal excretion, mostly in the form or idarubicinol.

Studies of cellular (nucleated and bone marrow blood cells) drug concentrations in leukaemic patients have shown that peak cellular idarubicin concentrations are reached a few minutes after injection.

Idarubicin and idarubicinol concentrations 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.

Paediatric Population:

Pharmacokinetic measurements in 7 paediatric patients receiving intravenous idarubicin in doses ranging from 15 to 40 mg/m^2/3 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).

In a separate study, pharmacokinetic measurements in 15 paediatric patients receiving oral idarubicin in doses ranging from 30 to 50 mg/m^2/ during the 3 days of treatment, the maximum plasma concentration of idarubicin was 10.6 ng/mL (range 2.7 – 16.7 ng/mL at the 40 mg/m^2 dose). The median terminal half-life of idarubicin was 9.2 hrs (range: 6.4 – 25.5 hrs). Significant accumulation of idarubicinol was seen over the 3 day treatment period. The observed terminal half-life value of idarubicin after IV was comparable to that following oral administration in paediatric patients.

Since C_{max} of idarubicin is similar in children and adults following oral administrations, absorption kinetics seem not to differ between adults and children.

Following both oral and IV administrations, the elimination half-life values of idarubicin in children and adults differ:

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.

5.3 Preclinical safety data

The LD50 (median values) intravenous idarubicin was 4.4 mg / kg in mice, 2.9 mg / kg in rats and about 1.0 mg / kg in dogs. The main targets after a single dose were hemolymphopoietic system, especially dogs, the gastrointestinal tract. Toxic effects in rats and dogs after repeated intravenous administration of idarubicin were investigated. The main target of intravenous idarubicin in the above species were hemolymphopoietic system, gastrointestinal tract, kidney, liver, and male and female reproductive organs.

In relation to the heart, subacute and cardiotoxicity studies indicate that intravenous idarubicin was mild to moderately cardiotoxic only lethal doses, whereas doxorubicin and daunorubicin clear even cause myocardial changes to non-lethal doses.

Idarubicin was genotoxic in most in vitro or in vivo performed. Intravenous idarubicin was toxic to the reproductive organs, and embryotoxic and teratogenic in rats. No effects were detected worthy of mention in both mothers and in the progeny of mice which have been administered doses up to 0.2 mg/kg/day during the perinatal and postnatal periods. It is unknown whether the compound is excreted in breast milk. Intravenous idarubicin, such as anthracyclines and other cytotoxic drugs, was carcinogenic in rats. A local safety study in dogs showed that the drug causes tissue necrosis from extravasation.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerol,

Hydrochloric acid, concentrate,

Sodium hydroxide (for pH adjustment),

Water for injections.

6.2 Incompatibilities

Prolonged contact with any alkaline pH solution must be avoided, since it can give rise to drug degradation. Idarubicin hydrochloride must not be mixed with heparin as it may form a precipitate.

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C). Store in the original package in order to protect from light.

6.5 Nature and contents of container

Colourless Type I glass vial with chlorobutyl rubber stopper, sealed with an aluminium cap with an orange plastic “flip-off” cap.

1 vial with 20 ml solution for injection

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Idarubicin Accord solution must only be administered intravenously via an infusion line with a freely running intravenous infusion of 0.9% sodium chloride over a period of 5 to 10 minutes.

This method minimises the risks of thrombosis and perivascular extravasation which can lead to severe cellulitis and necrosis. Phlebosclerosis can result from injection into small veins or repeated injections into the same vein.

The following recommendations for protection are given, due to the toxic nature of this substance:

- Personnel must be trained in the correct handling method

- Pregnant women must be excluded from working with this drug

- Personnel handling the drug must wear protective clothing: eyewear, overalls, disposable gloves and masks

- A work area should be set up with a surface protected with absorbent paper, plasticised on one side

- All instruments used for administration or cleaning, including gloves, must be disposed of in high-risk containers for incineration at high temperatures

Spills or leaks must be treated with dilute sodium hypochlorite solution (1% chlorine) and then with water.

All cleaning materials must then be disposed of as described above.

Accidental contact with skin or eyes must be treated immediately by washing thoroughly with water, soap and water, or sodium bicarbonate solution; medical attention may be necessary. Discard any unused solution.

Any remaining medicine, as well as all the materials that were used for its reconstitution, dilution and administration, must be destroyed in accordance with the hospital procedure applicable for cytotoxic agents and in compliance with current legislation relating to the elimination of hazardous waste.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 20075/0526

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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