SCHEDULING STATUS: S4

PROPRIETARY NAME (and dosage form):

FARMORUBICIN® CSV 10 mg/5 ml (injection)

FARMORUBICIN® CSV 20 mg/10 ml (injection)

FARMORUBICIN® CSV 50 mg/25 ml (injection)

FARMORUBICIN® CSV 200 mg/100 ml (injection)

COMPOSITION:

Each vial contains:

FARMORUBICIN CSV 10 mg/5 ml: Epirubicin HCl 10 mg (2 mg/ml)

FARMORUBICIN CSV 20 mg/10 ml: Epirubicin HCl 20 mg (2 mg/ml)

FARMORUBICIN CSV 50 mg/25 ml: Epirubicin HCl 50 mg (2 mg/ml)

FARMORUBICIN CSV 200 mg/100 ml: Epirubicin HCl 200 mg (2 mg/ml)

Excipients: Sodium chloride, hydrochloric acid, water for injection

PHARMACOLOGICAL CLASSIFICATION:

A26 Cytostatic agents

PHARMACOLOGICAL ACTION:

Epirubicin is an anthracycline antibiotic with antineoplastic activity. This mechanism of action is related to its ability to bind to DNA.

Cell culture studies have shown rapid cell penetration, localisation in the nucleus and inhibition of nucleic acid synthesis and mitosis.

In patients with normal hepatic and renal function, plasma levels after I.V. injection of 75 - 90 mg/m² of the medicine follow a tri-exponential decreasing pattern with a very fast first phase and a slow terminal phase with a mean half-life of about 40 hours. Plasma levels of the component's main metabolite, the 13-0H derivative, are constantly lower and virtually parallel to those of the unchanged medicine.

Epirubicin is eliminated mainly through the liver: high plasma clearance values (0,9 l/min) indicated that this slow elimination is due to extensive tissue distribution. The medicine does not cross the blood-brain barrier.

INDICATIONS:

FARMORUBICIN CSV is indicated for the treatment of the following:

- Breast cancer
- Gastric cancer
- Non small cell lung carcinoma
- Non-Hodgkin's lymphoma
- Hodgkin's lymphoma
- Ovarian cancer
- Colorectal cancer
- Soft tissue sarcomas
- Malignant melanoma

CONTRA-INDICATIONS:

Hypersensitivity to FARMORUBICIN CSV or any other component of the product, other anthracyclines or anthracenediones.

Intravenous use:

- persistant myelosuppression
- severe hepatic impairment
- severe myocardial insufficiency
- recent myocardial infarction
- severe dysrhythmias
- previous treatments with maximum cumulative doses of epirubicin and/or other anthracyclines and anthracenediones (see WARNINGS)

WARNINGS:

1. Severe local tissue necrosis will occur if there is extravasation during administration (See SPECIAL PRECAUTIONS). FARMORUBICIN CSV must not be given by the intramuscular or subcutaneous route.

2. Myocardial toxicity, manifested in its most severe form by potentially fatal congestive heart failure (CHF), may occur either during therapy with FARMORUBICIN CSV 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 FARMORUBICIN CSV 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 FARMORUBICIN CSV may occur at lower cumulative doses whether or not cardiac risk factors are present.

3. Secondary acute myelogenous leukaemia (AML) has been reported in patients with breast cancer treated with anthracyclines, including FARMORUBICIN CSV. The occurrence of refractory secondary leukaemia is more common when such medicines are given in combination with DNA-damaging antineoplastic agents, when patients have been heavily pretreated with cytotoxic medicines, or when doses of FARMORUBICIN CSV have been escalated.

The cumulative risk of developing treatment-related AML, in 3844 patients with breast cancer who received adjuvant treatment with epirubicin-containing regimens, was estimated as 0,2 % at 3 years and 0,8 % at 5 years.

4. Dosage should be reduced in patients with impaired hepatic function (see DOSAGE AND DIRECTIONS FOR USE).

5. Severe myelosuppression may occur.

6. FARMORUBICIN CSV should be administered only under the supervision of a medical practitioner who is experienced in the use of cancer chemotherapeutic agents.

FARMORUBICIN CSV Injection should be administered only under the supervision of qualified medical practitioner experienced in the use of cytotoxic therapy. Before beginning treatment with FARMORUBICIN CSV, patients should recover from acute toxicities (such as stomatitis, neutropenia, thrombocytopenia, and generalised infections) of prior cytotoxic treatment.
Also, initial treatment with FARMORUBICIN CSV should be preceded by a careful baseline assessment of blood counts; serum levels of total bilirubin, AST and creatinine; and cardiac function as measured by left ventricular ejection function (LVEF). Patients should be carefully monitored during treatment for possible clinical complications due to myelosuppression. Supportive care may be necessary for the treatment of severe neutropenia and severe infectious complications. Monitoring for potential cardiotoxicity is also important, especially with greater cumulative exposure to FARMORUBICIN CSV.

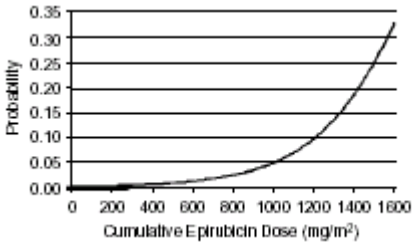
Haematologic Toxicity: A dose-dependent, reversible leukopenia and/or neutropenia is the predominant manifestation of haematologic toxicity associated with FARMORUBICIN CSV and represents the most common acute dose-limiting toxicity of FARMORUBICIN CSV. In most cases, the white blood cell (WBC) nadir is reached 10 to 14 days from FARMORUBICIN CSV administration.
Leukopenia/neutropenia is usually transient, with WBC and neutrophil counts generally returning to normal values by Day 21 after FARMORUBICIN CSV administration. FARMORUBICIN CSV at the recommended dose in combination with cyclophosphamide and fluorouracil can produce severe leukopenia and neutropenia.
Severe thrombocytopenia and anaemia may also occur. Clinical consequences of severe myelosuppression include fever, infection, septicaemia, septic shock, haemorrhage, tissue hypoxia, symptomatic anaemia, or death. If myelosuppressive complications occur, appropriate supportive measures (e.g., intravenous antibiotics, colony-stimulating factors, transfusions) may be required. Myelosuppression requires careful monitoring. Total and differential WBC, red blood cell (RBC) and platelet counts should be assessed before and during each cycle of therapy with FARMORUBICIN CSV.

Cardiac Function: Cardiotoxicity is a known risk of anthracycline treatment such as FARMORUBICIN CSV. Anthracycline-induced cardiac toxicity may be manifested by early (acute) or late (delayed) events. Early cardiac toxicity of FARMORUBICIN CSV consists mainly of sinus tachycardia and/or ECG abnormalities such as non-specific ST-T wave changes, but tachydysrhythmias, 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 considered an indication for the suspension of FARMORUBICIN CSV treatment.

Delayed cardiac toxicity results from a characteristic cardiomyopathy that is manifested by reduced LVEF and/or signs and symptoms of congestive heart failure (CHF) such as tachycardia, dyspnoea, pulmonary oedema, dependent oedema, hepatomegaly, ascites, pleural effusion, gallop rhythm. Life-threatening CHF is the most severe form of FARMORUBICIN CSV-induced cardiomyopathy. This toxicity appears to be dependent on the cumulative dose of FARMORUBICIN CSV and represents the cumulative dose-limiting toxicity of FARMORUBICIN CSV. If it occurs, delayed cardiotoxicity usually develops late in the course of therapy with FARMORUBICIN CSV or within 2 to 3 months after completion of treatment, but later events (several months to years after treatment termination) have been reported.

In a retrospective survey, including 9144 patients, mostly with solid tumours in advanced stages, the probability of developing CHF increased with increasing cumulative doses of FARMORUBICIN CSV (Figure below). The estimated risk of FARMORUBICIN CSV**-**treated patients developing clinically evident CHF was 0,9 % at a cumulative dose of 550 mg/m², 1,6 % at 700 mg/m², and 3,3 % at 900 mg/m². The risk of developing CHF in the absence of other cardiac risk factors increased steeply after a FARMORUBICIN CSV cumulative dose of 900 mg/m².

Risk of CHF in 9144 Patients Treated with Epirubicin



In another retrospective survey of 469 epirubicin-treated patients with metastatic or early breast cancer, the reported risk of CHF was comparable to that observed in the larger study of over 9000 patients. Given the risk of cardiomyopathy, a cumulative dose of 900 mg/m² FARMORUBICIN CSV should be exceeded only with extreme caution. Risk factors (active or dormant cardiovascular disease, prior or concomitant radiotherapy to the mediastinal/pericardial area, previous therapy with other anthracyclines or anthracenediones, concomitant use of other medicines with the ability to suppress cardiac contractility) may increase the risk of cardiac toxicity. Although not formally tested, it is probable that the toxicity of FARMORUBICN CSV and other anthracyclines or anthracenediones is additive. Cardiac toxicity with FARMORUBICIN CSV may occur at lower cumulative doses whether or not cardiac risk factors are present.

Although endomyocardial biopsy is recognised as the most sensitive diagnostic tool to detect FARMORUBICIN CSV-induced cardiomyopathy, this invasive examination is not practically performed on a routine basis. Electrocardiogram (ECG) changes such as dysrhythmias, a reduction of the QRS voltage, or a prolongation beyond normal limits of the systolic time interval may be indicative of FARMORUBICIN CSV-induced cardiomyopathy, but ECG is not a sensitive or specific method for following FARMORUBICIN CSV-related cardiotoxicity.

The risk of serious cardiac impairment may be decreased through regular monitoring of LVEF during the course of treatment with prompt discontinuation of FARMORUBICIN CSV at the first sign of impaired function.

The preferred method for repeated assessment of cardiac function is evaluation of LVEF measured by multi-gated radionuclide angiography (MUGA) or echocardiography (ECHO). A baseline cardiac evaluation with an ECG and a MUGA scan or an ECHO is recommended, especially in patients with risk factors for increased cardiac toxicity. Repeated MUGA or ECHO determinations of LVEF should be performed, particularly with higher, cumulative

FARMORUBICIN CSV doses. The technique used for assessment should be consistent through follow-up. In patients with risk factors, particularly prior anthracycline or anthracenedione use, the monitoring of cardiac function must be particularly strict and the risk-benefit of continuing treatment with FARMORUBICIN CSV in patients with impaired cardiac function must be carefully evaluated.

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 other medicines with the ability to suppress cardiac contractility or cardiotoxic medicines (e.g trastuzumab). Anthracyclines including FARMORUBICIN CSV should not be administered in combination with other cardiotoxic agents unless the patients' cardiac function is closely monitored. Patients receiving FARMORUBICIN CSV 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, medical practitioner should avoid FARMORUBICIN CSV-based therapy for up to 24 weeks after stopping trastuzumab when possible. If FARMORUBICIN CSV is used before this time, careful monitoring of cardiac function is recommended.

Secondary Leukaemia*:* The occurrence of secondary acute myelogenous leukaemia, with or without a preleukaemic phase, has been reported in patients treated with FARMORUBICIN CSV. Secondary leukaemia is more common when such medicines are given in combination with DNA-damaging antineoplastic agents, when patients have been heavily pretreated with cytotoxic medicines or when doses of the FARMORUBICIN CSV have been escalated. These leukaemias can have a short 1 to 3 year latency period. An analysis of 3844 patients who received adjuvant treatment with epirubicin in controlled clinical trials, showed a cumulative risk of secondary acute myelogenous leukemia of about 0,2 % (approximate 95 % CI, 0,05 - 0,4) at 3 years and approximately 0,8 % (approximate 95 % CI, 0,3 - 1,2) at 5 years. FARMORUBICIN CSV is mutagenic, clastogenic and carcinogenic in animals (see next section, Carcinogenesis, Mutagenesis and Impairment of Fertility).

Carcinogenesis, Mutagenesis & Impairment of Fertility*:* Treatment-related acute myelogenous leukaemia has been reported in women treated with FARMORUBICIN CSV-based adjuvant chemotherapy regimens (see above section, WARNINGS, Secondary Leukaemia). Conventional long-term animal studies to evaluate the carcinogenic potential of epirubicin have not been conducted, but intravenous administration of a single 3,6 mg/kg epirubicin dose to female rats (about 0,2 times the maximum recommended human dose on a body surface area basis) approximately doubled the incidence of mammary tumours (primarily fibroadenomas) observed at 1 year. Administration of 0,5 mg/kg epirubicin intravenously to rats (about 0,025 times the maximum recommended human dose on a body surface area basis) every 3 weeks for ten doses increased the incidence of subcutaneous fibromas in males over an 18-month observation period. In addition, subcutaneous administration of 0,75 or 1,0 mg/kg/day (about 0,015 times the maximum recommended human dose on a body surface are a basis) to newborn rats for 4 days on both the first and tenth day after birth for a total of eight doses increased the incidence of animals with tumours compared to controls during a 24-month observation period. Epirubicin such as contained in FARMORUBICIN CSV was mutagenic *in vitro* to bacteria (Ames test) either in the presence or absence of metabolic activation and to mammalian cells (HGPRT assay in V79 Chinese hamster lung fibroblasts) in the absence but not in the presence of metabolic activation. Epirubicin such as contained in FARMORUBICIN CSV was clastogenic *in vitro* (chromosome aberrations in human lymphocytes) both in the presence and absence of metabolic activation and was also clastogenic *in vivo* (chromosome aberration in mouse bone marrow).

In fertility studies in rats, males were given epirubicin daily for 9 weeks and mated with females that were given epirubicin daily for 2 weeks prior to mating and through Day 7 of gestation. When 0,3 mg/kg/day (about 0,015 times the maximum recommended human single dose on a body surface area basis) was administered to both sexes, no pregnancies resulted. No effects on mating behaviour or fertility were observed at 0,1 mg/kg/day, but male rats had atrophy of the testes and epididymis, and reduced spermatogenesis. The 0,1 mg/kg/day dose also caused embryolethality. An increased incidence of foetal growth retardation was observed in these studies at 0,03 mg/kg/day (about 0,0015 times the maximum recommended human single dose

on a body surface area basis). Multiple daily doses of epirubicin to rabbits and dogs also caused atrophy of male reproductive organs. Single 20,5 and 12 mg/kg doses of intravenous epirubicin caused testicular atrophy in mice and rats, respectively (both approximately 0,5 times the maximum recommended human dose on a body surface area basis). A single dose of 16,7 mg/kg epirubicin caused uterine atrophy in rats. Although experimental data are not available, FARMORUBICIN CSV could induce chromosomal damage in human spermatozoa due to its genotoxic potential. Men undergoing treatment with FARMORUBICIN CSV should use effective contraceptive methods. FARMORUBICIN CSV may cause irreversible amenorrhoea (premature menopause) in premenopausal women.

Liver Function*:* The major route of elimination of FARMORUBICIN CSV is the hepatobiliary system. Serum total bilirubin and AST levels should be evaluated before and during treatment with FARMORUBICIN CSV.

Patients with elevated bilirubin or AST may experience slower clearance of medicine with an increase in overall toxicity. Lower doses are recommended in these patients (see DOSAGE AND DIRECTIONS FOR USE). Patients with severe hepatic impairment have not been evaluated; therefore, FARMORUBICIN CSV should not be used in this patient population.

Renal Function*:* Serum creatinine should be assessed before and during therapy. Dosage adjustment is necessary in patients with serum creatinine >5 mg/dL (see DOSAGE AND DIRECTIONS FOR USE). Patients undergoing dialysis have not been studied.

Tumour-Lysis Syndrome*:* FARMORUBICIN CSV may induce hyperuricaemia as a consequence of the extensive purine catabolism that accompanies drug-induced rapid lysis of highly chemosensitive neoplastic cells (tumour lysis syndrome). Other metabolic abnormalities may also occur. While not generally a problem in patients with breast cancer, medical practitioner should consider the potential for tumour-lysis syndrome in potentially susceptible patients and should consider monitoring serum uric acid, potassium, calcium, phosphate and creatinine immediately after initial chemotherapy administration. Hydration, urine alkalinisation and

prophylaxis with allopurinol to prevent hyperuricaemia may minimise potential complications of tumour-lysis syndrome.

INTERACTIONS:

FARMORUBICIN CSV is mainly used in combination with other cytotoxic medicines. Additive toxicity may occur especially with regard to bone marrow/haematologic and gastro-intestinal effects (see WARNINGS). The use of FARMORUBICIN CSV in combination chemotherapy with other potentially cardiotoxic medicines, as well as the concomitant use of other cardioactive compounds (e.g. calcium channel blockers), requires monitoring of cardiac function throughout treatment.

Cimetidine increased the AUC of Farmorubicin CSV by 50 % and should be stopped during treatment with FARMORUBICIN CSV.

FARMORUBICIN CSV is extensively metabolised by the liver. Changes in hepatic function induced by concomitant therapies may affect FARMORUBICIN CSV metabolism, pharmacokinetics, therapeutic efficacy and/or toxicity.

When given prior to FARMORUBICIN CSV, paclitaxel can cause increased plasma concentrations of unchanged FARMORUBICIN CSV and its metabolites, the latter being, however, neither toxic nor active. Coadministration of paclitaxel or docetaxel did not affect the pharmacokinetics of FARMORUBICIN CSV when FARMORUBICIN CSV was administered prior to the taxane.

PREGNANCY AND LACTATION:

FARMORUBICIN CSV is teratogenic to animals and is contra-indicated in pregnancy, and to mothers who are breastfeeding.

Impairment of Fertility:

FARMORUBICIN CSV could induce chromosomal damage in humans' spermatozoa. Men undergoing treatment with FARMORUBICIN CSV should use effective contraceptive methods.

FARMORUBICIN CSV may cause amenorrhoea or premature menopause in premenopausal women.

Lactation:

It is not known whether FARMORUBICIN CSV is excreted in human milk. Because many medicines, including other anthracyclines, are excreted in human milk and because of the potential for serious adverse reactions in breastfeeding infants from FARMORUBICIN CSV, mothers should discontinue breastfeeding prior to taking FARMORUBICIN CSV.

DOSAGE AND DIRECTIONS FOR USE:

FARMORUBICIN CSV is usually administered by intravenous injection.
It is not active when given orally and should not be injected intramuscularly or intrathecally.

Intravenous (IV) administration:

Standard starting dose regimen:

When FARMORUBICIN CSV is used as a single agent, the recommended dosage in adults is 60 - 90 mg/m² body area. The total starting dose per cycle may be given as a single dose or divided over 2 - 3 successive days. The medicine should be injected I.V. in 3 - 5 minutes and, depending on the patient's haematological status, the dose should be repeated at 21-day intervals (every 3 - 4 weeks).

Higher starting dose regimen:

Doses of 90 to 135 mg/m² as single agent and 90 to 120 mg/m² in combination therapy, every 3 - 4 weeks may be used in the treatment of advanced breast cancer and lung cancer.
Lower doses, 60 - 75 mg/m² are recommended for patients whose bone marrow function has already been impaired by earlier chemotherapy or radiotherapy, by age, or by bone marrow neoplastic infiltrations. The total dosage per cycle may be divided over 2 - 3 successive days. When FARMORUBICIN CSV is used in association with other anti-tumour agents, the doses need to be adequately reduced.

Hepatic dysfunction:

Since the major route of elimination of FARMORUBICIN CSV is the hepatobiliary system the dosage should be reduced in patients with impaired liver function, in order to avoid an increase of overall toxicity. The dosage should be adjusted as follows:
(a) Moderate liver impairment – Bilirubin 24 - 51,3 mmol/l (1,4 - 3 mg/100 ml) or BSP retention:

9 - 15 % - requires a 50 % reduction of dose.

(b) Severe liver impairment – Bilirubin >51,3 mmol/l (>3 mg/100 ml) or BSP retention:

>15 % - necessitates a dose reduction of 75 %.

Renal dysfunction:

Moderate renal impairment does not appear to call for a dose reduction in view of the limited amount of FARMORUBICIN CSV excreted via this route. Lower starting doses should be considered in patients with severe renal impairment (serum creatinine > 5 mg/dl).

Incompatibilities:

Prolonged contact with any solution of an alkaline pH should be avoided as it will result in hydrolysis of FARMORUBICIN CSV.

FARMORUBICIN CSV should not be mixed with heparin due to chemical incompatibility that may lead to precipitation.

FARMORUBICIN CSV should not be mixed with other medicines in the same syringe.

Intravenous administration:

It is advisable to administer the FARMORUBICIN CSV via the tubing of a freely-flowing I.V. infusion (0,9 % sodium chloride or 5 % glucose solution) after checking that the needle is well placed in the vein. The usual infusion times range between 3 and 20 minutes depending upon dosage and volume of the infusion solution. This method minimises the risk of thrombosis and perivenous extravasation and makes sure the vein is flushed with saline after the administration of FARMORUBICIN CSV.

A direct push injection is not recommended due to the risk of extravasation. Extravasation of FARMORUBICIN CSV from the vein during injection may give rise to severe tissue lesions, even necrosis.

Venous sclerosis may result from injection into small vessels or repeated injections within the same vein.

Protective measures:

N.B.: A designated area, preferably under laminar flow system, should be defined for reconstitution. The work surface should be protected with a disposable plastic-backed absorbent paper. All items used for reconstitution should be placed in high-risk, waste-disposable bags for high temperature incineration. It is advisable that personnel handling FARMORUBICIN CSV should wear gloves. Accidental contact of FARMORUBICIN CSV solution with skin or mucosa should be treated immediately by copious lavage with soap and water. The conjunctiva should be washed with saline solution.

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

Side Effects:

FARMORUBICIN CSV causes pronounced bone-marrow depression.

The other side effects were categorised utilising the incidence rate as follows:

Very common: ≥1/10 (≥10%)

Common: ≥1/100 and <1/10 (≥1% and <10%)

Uncommon: ≥1/1000 and <1/100 (≥0,1% and <1%)

Serious drug-related adverse events that occurred during clinical trials are tabulated below:

System Organ Class	***Frequency***	***Adverse Events***
Blood and lymphatic system disorders	**Very common**	Leukopenia, neutropenia, anaemia, thrombocytopenia
Cardiac disorders	**Common**	Asymptomatic drops in left ventricular ejection fraction (LVEF), congestive heart failure (CHF)
Reproductive system and breast disorders	**Common**	Amenorrhoea
Eye disorders	**Uncommon**	Conjunctivitis/keratitis
Gastrointestinal disorders	**Common**	Nausea/vomiting, mucositis/stomatitis, diarrhoea
Metabolism and nutrition disorders	**Common**	Anorexia
Infections and infestations	**Very common**	Infection
Neoplasms benign and malignant leukemia	**Uncommon**	Acute lymphocytic leukaemia, acute myelogenous leukaemia

System Organ Class	*Frequency*	*Adverse Events*
Skin and subcutaneous tissue disorders	**Common**	Alopecia, local toxicity, rash/itch, skin changes
Vascular disorders	**Uncommon**	Hot flushes
General disorders and administrative site conditions	**Common**	Malaise/asthenia, fever
Investigations	**Rare**	Changes in transaminase levels

Adverse events which occurred during postmarketing surveillance:

System Organ Class	*Frequency*	*Adverse Events*
Gastrointestinal disorders	**Common**	Pain or burning sensation, erythema, dehydration
	Uncommon	Erosions, ulceration, bleeding, hyperpigmentation of the oral mucosa
Immune system disorders	**Uncommon**	Anaphylaxis
Renal and urinary disorders	**Common**	Red colouration of urine for 1 to 2 days after administration
Skin and subcutaneous tissue disorders	**Uncommon**	Flushes, skin and nail hyperpigmentation, hypersensitivity to irradiated skin (radiation recall reaction), photosensitivity, urticaria
Vascular disorders	**Uncommon**	Phlebitis, thrombophlebitis, thromboembolism, shock
Metabolism and nutrition disorders	**Rare**	Dehydration

Special Precautions:

During the first cycles of treatment with FARMORUBICIN CSV patients must be carefully and frequently monitored. White and red blood cell and platelet counts should be carefully monitored.

FARMORUBICIN CSV should be given with great care in reduced doses to elderly patients and those with hepatic impairment. Before commencing treatment and if possible during treatment, liver function should be evaluated (AST, ALT, alkaline phosphatase, bilirubin, BSF).

Immunosuppressant Effects/Increased susceptibility of Infections:

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

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Acute overdosage with FARMORUBICIN CSV will result in severe myelosuppression (mainly leukopenia and thrombocytopenia), gastrointestinal toxic effects (mainly mucositis) and acute cardiac complications. Treatment is supportive and symptomatic.

IDENTIFICATION:

Clear red solution practically free from particles.

PRESENTATION:

Vials of 10 mg, 20 mg, 50 mg and 200 mg.

STORAGE INSTRUCTIONS:

Store between 2 - 8 °C. Protect from light. Do not freeze. Single dose preparation - discard any unused portion.

Keep out of reach of children.

REGISTRATION NUMBER:

FARMORUBICIN® CSV 10 mg/5 ml: 32/26/0600

FARMORUBICIN® CSV 20 mg/10 ml: 32/26/0601

FARMORUBICIN® CSV 50 mg/25 ml: 32/26/0602

FARMORUBICIN® CSV 200 mg/100 ml: 32/26/0603

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Pfizer Laboratories (Pty) Ltd.

85 Bute Lane

Sandton

2196

DATE OF PUBLICATION OF THIS PACKAGE INSERT:

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