PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

[Pr]**IDAMYCIN® PFS®**

idarubicin hydrochloride injection

Preservative Free Solution, 1 mg/mL Idarubicin hydrochloride (5 mg/5mL, 10 mg/10mL, 20 mg/20mL), intravenous injection

House Standard

Antineoplastic Agent

Pfizer Canada ULC

17,300 Trans-Canada Highway

Kirkland, Quebec, H9J 2M5

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RECENT MAJOR LABEL CHANGES

7 Warnings and Precautions, Embryo-Fetal Toxicity and Teratogenic Risk; 7.1.1 Pregnant Women; 7.1.2 Breastfeeding	03/2022

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

IDAMYCIN PFS (idarubicin hydrochloride injection) is indicated, alone or in combination chemotherapy regiments involving other cytotoxic agents, for:

- 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.

1.1 Pediatrics

Pediatrics (age range not specified): IDAMYCIN PFS is indicated in acute lymphocytic leukemia (ALL) as second line treatment in children. [see **1 INDICATIONS**]

1.2 Geriatrics

Geriatrics (≥ 60 years): Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety or effectiveness. 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.

2 CONTRAINDICATIONS

IDAMYCIN PFS is contraindicated in

- patients who are hypersensitive to idarubicin or to any ingredient in the formulation or component of the container. For a complete listing, see **6 DOSAGE FORMS, COMPOSITION AND PACKAGING;**
- Hypersensitivity to any other anthracyclines or anthracenediones such as Pharmorubicin PFS (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 **7 WARNINGS AND PRECAUTIONS**)

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions
• Myelosuppression (see **7 Warnings and Precautions, Hematologic**) • Cardiotoxicity (see **7 Warnings and Precautions, Cardiovascular**)

4 DOSAGE AND ADMINISTRATION

As with all parenteral products, intravenous solution should be inspected visually for clarity, particulate matter, precipitate, discolouration and leakage prior to administration. Solution showing haziness, particulate matter, precipitate, discolouration or leakage should not be used and unused portions should be discarded.

4.1 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 **7 WARNINGS AND PRECAUTIONS**).

The total dose of IDAMYCIN PFS (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

4.2 Recommended Dose and Dosage Adjustment

Intravenous

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^2 daily by intravenous injection for 3 days in combination with cytarabine, or

(b) 8 mg/m^2 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^2 daily by intravenous injection for 3 days as a single agent, or

(b) in children, 10 mg/m^2 daily by intravenous injection for 3 days as a single agent.

4.4 Administration

IDAMYCIN PFS (idarubicin hydrochloride injection) **must not** be administered by intramuscular or subcutaneous injection. Unless specific compatibility data are available, IDAMYCIN PFS 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.

IDAMYCIN PFS 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 **7 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.

5 OVERDOSAGE

Very high doses of IDAMYCIN PFS 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.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intravenous injection	Solution for injection 1 mg / mL	Glycerol USP/Ph. Eur. Hydrochloric acid NF Water for injection USP

IDAMYCIN PFS is a clear, red-orange, aqueous, preservative-free solution, free from visible particles containing 1 mg/mL idarubicin hydrochloride. The solution is filled in glass vials. The vial and vial stopper are not manufactured with natural rubber latex.

IDAMYCIN PFS is available in 5 mL, 10 mL, and 20 mL vials. The 5 mL, 10 mL, and 20 mL vials are packaged and supplied in a single vial carton.

7 WARNINGS AND PRECAUTIONS

Please see **3 SERIOUS WARNINGS AND PRECAUTIONS BOX.**

General

Therapy with IDAMYCIN PFS requires close observation of the patient and laboratory monitoring. Idarubicin may induce hyperuricemia as a consequence of the extensive purine catabolism that accompanies drug-induced rapid lysis of neoplastic cells ('tumour 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 tumour 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 hydrochloride.

Extravasation of IDAMYCIN PFS 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 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.

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 (see **16 NON-CLINICAL TOXICOLOGY)**.

Cardiovascular

Cardiotoxicity is a risk of anthracycline treatment that may be manifested by early (i.e., acute) or late (ie, 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 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.** Available data on patients treated with oral idarubicin hydrochloride 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 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 reported half-life of trastuzumab is approximately 28-38 days. Trastuzumab may persist in the circulation for up to 7 months. Therefore, physicians should avoid anthracycline-based therapy for up to 7 months 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 IDAMYCIN PFS 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 IDAMYCIN PFS 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. 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 **4 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

IDAMYCIN PFS 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

IDAMYCIN PFS 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).

Immune

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.

Monitoring and Laboratory Tests

Therapy with IDAMYCIN PFS requires close observation of the patient and laboratory monitoring (see **7 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 **7 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 7 **WARNINGS AND PRECAUTIONS**, Hepatic/Biliary/Pancreatic and 7 **WARNINGS AND PRECAUTION** Renal).

Hematologic profiles should be assessed before and during each cycle of therapy with idarubicin including differential white blood cell (WBC) counts (see 7 **WARNINGS AND PRECAUTIONS**, Hematologic).

Renal

IDAMYCIN PFS 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).

Reproductive Health: Female and Male Potential

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 **(**see **7.1.1 Pregnant Women).**

- **Fertility**

  IDAMYCIN PFS can induce chromosomal damage in human spermatozoa. For this reason, males undergoing idarubicin treatment should use contraceptive measures. Both men and women should seek advice on fertility preservation before treatment.

- **Embryo-fetal Toxicity and Teratogenic Risk**

Idarubicin can cause genotoxicity. An effective method of contraception is required for both male and female patients during and for a period after treatment with idarubicin. Patients desiring to have children after completion of therapy should be advised to obtain genetic counselling if appropriate and available. There are no data on teratogenicity in humans. In animals, IDAMYCIM PFS is not teratogenic in the rabbit, even at toxic doses. However, it is teratogenic in the rat (see **16 NON-CLINICAL TOXICOLOGY**)

7.1 Special Populations

7.1.1 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.

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 IDAMYCIN PFS is to be used during pregnancy, or if the patient becomes pregnant during therapy.

Therefore, women of childbearing potential should be prescribed effective contraceptive methods and counselled on the risks of pregnancy.

Women of Childbearing Potential/ Contraception in Males and Females

Women of childbearing potential should be advised to avoid becoming pregnant during treatment. Women of childbearing potential should be advised 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.

7.1.2 Breast-feeding

It is not known whether idarubicin or its metabolites are excreted in human milk. Because many drugs, including other anthracyclines, are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from idarubicin, advise lactating women not to breastfeed during treatment with idarubicin and for at least 14 days after last dose.

7.1.3 Pediatrics

There are no specific warnings associated with pediatric use.

7.1.4 Geriatrics

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 **4 DOSAGE AND ADMINISTRATION** and **8 ADVERSE REACTIONS**).

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

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 intravenous 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%.

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

The clinical trial adverse reaction data is not available.

8.2.1 Clinical Trial Adverse Reactions – Pediatrics

The clinical trial adverse reaction data is not available.

8.3 Less Common Clinical Trial Adverse Reactions

The clinical trial adverse reaction data is not available.

8.3.1 Less Common Clinical Trial Adverse Reactions – Pediatrics

The clinical trial adverse reaction data is not available.

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Clinical Trial Findings

The clinical trial abnormal laboratory findings data is not available.

Post-Market Findings

The post-market abnormal laboratory findings data is not available.

8.5 Post-Market Adverse Reactions

Cardiovascular: sinus tachycardia, ECG abnormalities, tachyarrhythmias, atrio-ventricular and bundle branch block, asymptomatic reductions in LVEF, 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 **7 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 color 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

9 DRUG INTERACTIONS

9.3 Drug-Behavioural Interactions

There is no data on drug-behavioural interactions.

9.4 Drug-Drug Interactions

Idarubicin is a potent myelosuppressant and 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 **7 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.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 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.

10.2 Pharmacodynamics

This information is not available.

10.3 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 patients with normal renal and hepatic function, idarubicin is extensively metabolized to an active metabolite, idarubicinol.

Elimination:

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.

11 STORAGE, STABILITY AND DISPOSAL

IDAMYCIN PFS (idarubicin hydrochloride injection) should be stored at 2-8°C and protected from light. Discard unused solution.

Incompatibility:

Unless specific compatibility data are available, IDAMYCIN PFS 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.

Disposal:

All materials which have come in contact with IDAMYCIN PFS should be segregated in plastic bags, sealed and marked as hazardous waste, and incinerated at 1000°C or higher [see **12 Special Handling Instructions**].

12 SPECIAL HANDLING INSTRUCTIONS

Preparation and handling

1. Personnel should be trained in good techniques for reconstitution and 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 IDAMYCIN PFS 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, IDAMYCIN PFS may be detoxified by adding sodium hypochlorite solution (household bleach) to the vial, in sufficient quantity to decolourize 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 and disposable equipment in a safe manner. Thoroughly wash non-disposable equipment in soap and water.

Spillage/Contamination

Wear gloves, mask, protective clothing. Treat spilled 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.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

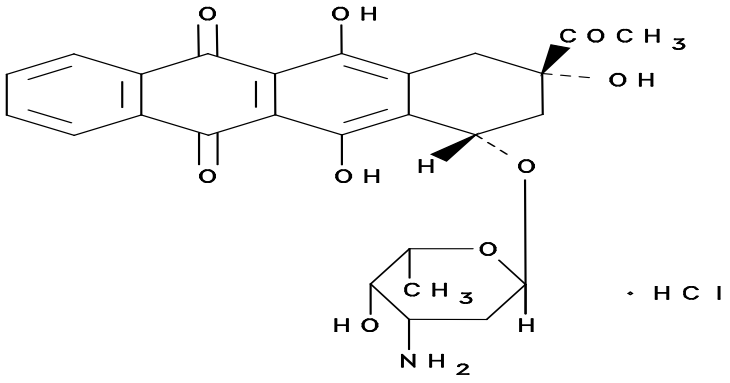
Drug Substance

Proper name: Idarubicin Hydrochloride

Chemical name: 5,12-Naphthacenedione, 9-acetyl-7-[(3-amino-2,3,6-trideoxy-α-L-*lyxo*-*h*exopyranosyl)oxy]-7,8,9,10-tetrahydro-6,9,11-trihydroxyhydrochloride, (7*S*-*cis*)-.

Molecular formula and molecular mass: $C_{26}H_{27}NO_9.HCl$; 533.95

Structural formula:



Physicochemical properties:

Idarubicin hydrochloride is a DNA intercalating analog of daunorubicin. The modification in position 4 of the aglycone, gives the compound a high lipophilicity.

It is a practically odourless red-orange powder. It is sparingly soluble in distilled water, slightly soluble in absolute ethanol and practically insoluble in non-polar organic solvents. Its melting point is 173-174°C.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

Four prospective randomized studies have been conducted to compare the efficacy and safety of idarubicin to that of daunorubicin, each in combination with cytarabine as induction therapy in previously untreated adult patients with acute non-lymphocytic leukemia (ANLL). Patients

who had persistent leukemia after the first induction course received a second course. These data are summarized in the following table:

Table 2 - Summary of patient demographics for clinical trials in ANLL

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
1 MSKCC*	Prospective randomized	12 mg/m^2 daily intravenously for 3 days, in combination with cytarabine 25 mg/m^2 bolus IV followed by 200 mg/m^2 daily x 5 days by continuous infusion	60 + 60	≤60 years	unknown
2 SEG**	Prospective randomized	12 mg/m^2 daily intravenously for 3 days, in combination with cytarabine 100 mg/m^2 daily x 7 days by continuous infusion	105 + 113	≥ 15 years	unknown
3 U.S. Multicenter	Prospective randomized	13 mg/m^2 daily intravenously for 3 days, in combination with cytarabine 100 mg/m^2 daily x 7 days by continuous infusion	101 +113	≥ 18 years	unknown
4 GIMEMA***	Prospective randomized	12 mg/m^2 daily intravenously for 3 days, in combination with cytarabine 100 mg/m^2 daily x 7 days by continuous infusion	124 + 125	≥ 55 years	unknown

*Memorial Sloan Kettering Cancer Center

**Southeastern Cancer Study Group

***Gruppo Italiano Malattie Ematologiche Maligne dell' Adulto

14.2 Study Results

The complete remission rates and medial survival times of the IDAMYCIN PFS + cytarabine treatment groups compared to the daunorubicin groups for the four studies are presented in Tables 3, 4, 5, and 6 below.

Table 3 - Results of study 1 (MSKCC) in ANLL

Primary Endpoints	Associated value and statistical significance for Drug at specific dosages	Associated value and statistical significance for Placebo or active control
Complete Remission Rate*	48/60 (80%)**	35/60 (58%)
Median Survival*	19.7 months**	13.5 months

* all patients randomized
**p < 0.05, unadjusted for prognostic factors or multiple endpoints

Table 4 - Results of study 2 (SEG) in ANLL

Primary Endpoints	Associated value and statistical significance for Drug at specific dosages	Associated value and statistical significance for Placebo or active control
Complete Remission Rate*	75/105 (71%)**	65/113 (58%)
Median Survival*	297 days	277 days

* all patients randomized
**p < 0.05, unadjusted for prognostic factors or multiple endpoints

Table 5 - Results of study 3 (U.S. Multicenter) in ANLL

Primary Endpoints	Associated value and statistical significance for Drug at specific dosages	Associated value and statistical significance for Placebo or active control
Complete Remission Rate*	68/101 (67%)	65/113 (58%)
Median Survival*	12.9 months**	8.7 months

* all patients randomized
**p < 0.05, unadjusted for prognostic factors or multiple endpoints

Table 6 - Results of study 4 (GIMEMA) in ANLL

Primary Endpoints	Associated value and statistical significance for Drug at specific dosages	Associated value and statistical significance for Placebo or active control
Complete Remission Rate*	50/124 (40%)	49/125 (39%)
Median Survival*	87 days	169 days

* all patients randomized

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology: In clinical oncology and in particular in the treatment of leukemia, which is and must be particularly aggressive, the maximum tolerable doses are normally used, and are, therefore, of the order of magnitude of the LD_{10} values, expressed in mg/m^2. These values are useful only when degree of exposure as expressed by the area under the curve (AUC) is also taken into consideration.

In the mouse, the LD_{10} of idarubicin hydrochloride was equal to 12.35 mg/m^2. The mouse:man exposure ratio at the same doses is estimated at approximately 5:1 to 10:1. In addition, the metabolism of idarubicin as compared with the less toxic idarubicinol, is more extensive in man than in the mouse. Idarubicinol was shown to be considerably less toxic than idarubicin. These results offer a considerably wide margin of safety for clinical use of idarubicin. Studies in the mouse also indicate that idarubicin is less cardiotoxic than either daunorubicin or doxorubicin when evaluated at dose ratios which result in similar antileukemic efficacy for the 3 drugs.

Studies were carried out with idarubicin in the rat and dog under the same experimental conditions in parallel with doxorubicin. In the rat, idarubicin was approximately twice as toxic as doxorubicin and had a greater effect on the haematolymphopoietic system. At the same time, idarubicin had a more limited effect on the myocardial, renal, hepatic and testicular parenchymae. In the dog, idarubicin was slightly more toxic than doxorubicin due to greater hematological effect, whereas doxorubicin had a greater effect on the renal, hepatic, testicular and myocardial parenchymae. The cardiotoxicity of idarubicin, when compared to its relative toxicity and activity, proved to be lower than that of doxorubicin.

Carcinogenicity: Idarubicin was studied on female Sprague-Dawley rats treated with a single intravenous dose of 1.8 mg/kg in comparison with doxorubicin administered as an equitoxic dose of 5 mg/kg. Results indicate that idarubicin must be considered to be carcinogenic, a characteristic which it shares with most other antitumoural drugs.

Reproductive and Developmental Toxicology: Idarubicin is not teratogenic in the rabbit, even at toxic doses. However, it is teratogenic in the rat at doses of 0.1 - 0.2 mg/kg/day or 0.7 - 1.4 mg/m^2.

Other toxicology: No long-term animal studies have been performed to evaluate genetic, juvenile, other specific toxicities associated with IDAMYCIN PFS.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr]IDAMYCIN® PFS®

Idarubicin Hydrochloride Injection

Read this carefully before you start taking **IDAMYCIN PFS** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **IDAMYCIN PFS**.

Serious Warnings and Precautions

- **Myelosuppression (bone marrow suppression leading to low blood cell and platelet counts):** Treatment with IDAMYCIN PFS can cause myelosuppression. This can lead to decreased white blood cells, decreased blood platelets, decreased red blood cells, fever, infections, hemorrhage (bleeding), tissue hypoxia, or even death.

- **Cardiotoxicity (damage to the heart):** Treatment with anthracyclines, such as IDAMYCIN PFS, can cause heart problems, especially in children. This can include:
  - irregular heartbeat rhythm or rate (arrhythmias),
  - atrioventricular and bundle branch block (partial or complete interruption of the electrical signal to the heart),
  - myocarditis/pericarditis (inflammation of the heart muscle and lining around the heart),
  - congestive heart failure (CHF; heart does not pump blood as well as it should); symptoms include:
    - dyspnea (shortness of breath),
    - pulmonary edema (excess fluid in the lungs), dependent edema (swelling in the lower body),
    - hepatomegaly (liver enlargement), oliguria (less pee than usual), ascites (fluid in the abdomen), and
    - pleural effusion (fluid around the lungs).

Your healthcare professional will monitor and assess the profile of your blood and how your heart is working before and during your treatment with IDAMYCIN PFS. If you develop myelosuppression or heart problems, they will act quickly to avoid and treat any unwanted effects and may stop your treatment if necessary. See the **Serious side effects and what to do about them table**, below, for more information on these and other serious side effects.

What is IDAMYCIN PFS used for?

IDAMYCIN PFS is used alone or in combination with other anti-cancer drugs:

- as a first line treatment for adults with acute non-lymphocytic leukemia (ANLL).
- as a treatment for adults with ANLL that has returned after treatment (relapsed) or does not respond to treatment (refractory).
- as a second line treatment for adults and children with acute lymphocytic leukemia (ALL).

How does IDAMYCIN PFS work?

IDAMYCIN PFS is an anti-cancer (cytotoxic) chemotherapy medication. It works by killing rapidly dividing cells, such as cancer cells, by interfering with the growth and division of these cells.

What are the ingredients in IDAMYCIN PFS?

Medicinal ingredient: Idarubicin hydrochloride

Non-medicinal ingredients: Glycerol, hydrochloric acid, and water for injection

IDAMYCIN PFS comes in the following dosage forms:

Preservative-Free Solution for injection: 1 mg / mL (in 5 mL, 10 mL, and 20 mL vials)

Do not use IDAMYCIN PFS if:

- you are allergic to idarubicin, any of the other ingredients in IDAMYCIN PFS, or its container.
- you are allergic to other anti-cancer drugs known as anthracyclines and anthracenediones (e.g., epirubicin, daunorubicin, mitoxanthrone, and mitomycin C).
- you have uncontrolled infections.
- you have persistent low blood cell and platelet counts (myelosuppression).
- you have severe liver problems.
- you have severe kidney problems.
- you have or have had severe heart problems including heart failure, a recent heart attack, or arrhythmia (irregular heartbeat).
- you have been treated with a maximum cumulative dose of idarubicin, doxorubicin, daunorubicin, epirubicin, other anthracyclines or other anthracenediones. If you are unsure ask your healthcare professional.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take IDAMYCIN PFS. Talk about any health conditions or problems you may have, including if you:

- have low blood cell counts;
- have an infection;
- have had radiation therapy (radiotherapy);
- Are pregnant or planning to become pregnant
- Are breast-feeding or planning to breast-feed
- have had unwanted effects from previous cancer treatment;
- have or have had heart and blood problems;
- have gastrointestinal problems (e.g., gastrointestinal bleeding or perforation);
- have liver problems;
- have kidney problems;
- are taking other anti-cancer medications (e.g., anthracyclines such as trastuzumab and anthracenediones);
- are taking medications that affect your heart (e.g., amlodipine, diltiazem, and verapamil);
- have had acute leukemia (a type of cancer of the blood or bone marrow) in the past;
- have had previous condition(s) or have previously taken medications that are known to lead to gastrointestinal problems. If you are unsure ask your healthcare professional;
- are planning to get a vaccine and have a compromised immune system. You may be at a higher risk of developing serious or fatal infections;
- are over the age of 60 years of age.

Other warnings you should know about:

IDAMYCIN PFS can cause serious side effects including:

- **Hyperuricemia (high uric acid levels in the blood):** Treatment with idarubicin can result in a large number of cancer cells dying and releasing their contents into the blood (also known as tumour lysis syndrome). This can lead to hyperuricemia. Your healthcare professional will monitor the profile of your blood (e.g., levels of uric acid, potassium, calcium, phosphate, and creatinine) before your treatment. They will suggest ways to prevent hyperuricemia (e.g., by staying hydrated), which may also help minimize the effects of tumour lysis syndrome.

- **Injury around the site of injection:** Extravasation (leakage of the injected solution that causes damage around the site of injection) can occur when IDAMYCIN PFS is given to you. This can lead to local pain, severe tissue lesions (e.g., a lump, bump, sore, or patch), severe local tissue necrosis (tissue death), and phlebosclerosis (a diseases

characterized by thickening or hardening of the walls of veins). If you develop extravasation, your healthcare professional will stop your treatment right away.

- **Blood clots:** The use of cytotoxic agents, such as idarubicin, has been reported to cause blood clots and thrombophlebitis (inflammation caused by blood clots, usually in the leg). Your healthcare professional will monitor your health for signs and symptoms of blood clots.

- **Secondary leukemia (a type of cancer that develops from previous disorders or exposure to cytotoxic agents):** Treatment with anthracyclines (cytotoxic agents), such as IDAMYCIN PFS, can lead to secondary leukemia. Your healthcare professional will monitor you for signs and symptoms of secondary leukemia.

- **Gastrointestinal problems:** Treatment with IDAMYCIN PFS can cause gastrointestinal problems including:
    - mucositis (inflammation and ulceration of the mucous membranes lining the digestive tract),
    - gastrointestinal perforation (a hole in the wall of your stomach or bowels), and
    - gastrointestinal bleeding (bleeding anywhere along the GI tract between mouth and anus).

  Your healthcare professional will monitor and assess your health before and during your treatment with IDAMYCIN PFS.

- **Kidney problems:** Treatment with IDAMYCIN PFS can cause kidney problems. You will have regular tests done before and during your treatment with IDAMYCIN PFS. These tests will tell your healthcare professional how your kidney is working.

See the **Serious side effects and what to do about them table**, below, for more information on these and other serious side effects.

Pregnancy and breastfeeding:

- Avoid becoming pregnant while taking IDAMYCIN PFS. If you are able to get pregnant or think you are pregnant, there are specific risks for your unborn baby that you must discuss with your healthcare professional.
- You and your partner should use effective birth control while taking IDAMYCIN PFS and for at least 6.5 months after your last dose.
- If you become pregnant or think you are pregnant while taking IDAMYCIN PFS, tell your healthcare professional right away.
- If you are breastfeeding or plan to breastfeed. It is not known if IDAMYCIN PFS passes into your breast milk. Do not breastfeed during treatment with IDAMYCIN PFS or for 14 days after your last dose. Talk to your healthcare professional about the best way to feed your baby during this time.

Fertility:

- IDAMYCIN PFS is a cytotoxic agent and can cause fertility impairment. If you are a male, it can damage the DNA in your sperm. You and your partner should use effective birth control while taking IDAMYCIN PFS and for at least 3.5 months after your last dose.
- If you want to become pregnant or father a child after treatment with IDAMYCIN PFS, talk to your healthcare professional about fertility preservation options before starting your treatment.
- Speak to your healthcare profession if you decide to have a child after completing your treatment with IDAMYCIN PFS. Your healthcare professional will advise you on whether genetic counselling would be appropriate for you.

Check-ups and testing:
You will have regular visits with your healthcare professional before, during, and after your treatment. They may do tests that will assess the profile of your blood, and how your heart, liver, and kidneys are working. This will help your healthcare professional assess your health and tell them how IDAMYCIN PFS is affecting you.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with IDAMYCIN PFS:

- chemotherapy medicines used to treat different types of cancers such as:
    - anthracyclines
    - anthracenediones
    - alkylating agents (e.g., cyclophosphamide)
    - antineoplastic agents (e.g., etoposide, cytarabine, and fludarabine)
    - cardiotoxic drugs (e.g., cyclophosphamide and paclitaxel)
    - cardioactive compounds (e.g., amlodipine, diltiazem, and verapamil)
- medicines known as corticosteroids that are used to reduce inflammation and suppress the immune system (e.g., dexamethasone).

How to take IDAMYCIN PFS:

Your healthcare professional will prepare and give you IDAMYCIN PFS. You may receive IDAMYCIN PFS through your veins (i.e., “intravenously” or “IV”). However, if you are getting multiple injections, your healthcare professional may use a catheter (thin tube) or port to inject medicines into your body.

Usual dose:

Your healthcare professional will determine the right dose, length, and cycle of IDAMYCIN PFS for you based on:

- your medical condition(s),
- treatment goals,
- the medicines (including chemotherapy) you are getting, and
- how your body responds to those medicines.

Overdose:

If you think you, or a person you are caring for, have been given too much IDAMYCIN PFS, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you miss your scheduled treatment with the drug, contact your doctor as soon as possible to schedule your next treatment.

What are possible side effects from using IDAMYCIN PFS?

These are not all the possible side effects you may have when taking IDAMYCIN PFS. If you experience any side effects not listed here, tell your healthcare professional.

Some side effects may include:

- hair loss (alopecia), which is temporary and usually starts to grow back within 2 or 3 months after you have finished your treatments.
- red colouration of your urine for 1 to 2 days after being given IDAMYCIN PFS.
- dehydration.
- inflammation of the skin where radiation was received (radiation recall reaction).
- hot flashes.
- skin and nail changes or colouration.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
COMMON			
Infection as a result of low white blood cell count: fever, chills, sweating, sore throat, nausea, vomiting, diarrhea, generally feeling unwell, coughing, redness or swelling around a cut, wound at catheter		✓	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
site, a burning feeling when you urinate, unusual vaginal itching or discharge			
Anemia (decreased number of red blood cells): weakness, dizziness, shortness of breath, fatigue, loss of energy, irregular heartbeats, pale complexion		✓	
RARE			
Cardiovascular problems (heart and blood problems including cardiac toxicity, congestive heart failure, low blood platelets)**:** rapid, slow or irregular heartbeat, chest pain, swelling of the ankles, legs or feet, shortness of breath, heart stops beating, palpitations, cough, fluid retention, lack of appetite, nausea, bruising or bleeding for longer than usual if you hurt yourself		✓	
Injection site reactions: pain, sores, burning at injection site, blistering, itching, redness, severe skin damage, tenderness, warmth in the area around the injection		✓	
Hemorrhage (increased bleeding from the blood vessels): dark urine or dark/bloody stool, unexplained bruising, headaches, weakness, tingling or numbness in the arms or legs, nausea, vomiting, changes in vision or balance		✓	
Colitis (bowel inflammation) or digestive tract bleeding: bloody stools, bloody vomit, severe or		✓	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
persistent diarrhea, abdominal pain, nausea and vomiting, fever			
UNKNOWN FREQUENCY			
Liver problems: yellowing of your skin and eyes (jaundice), right upper stomach area pain, swelling, nausea, vomiting, unusual dark urine, or unusual tiredness		✓	
Mucositis (inflammation and ulceration of the mucous membranes lining the digestive tract): painful, red, shiny or swollen gums, tongue, mouth or throat sores, blood in the mouth, difficult or painful swallowing or talking, dry mouth, mild burning, or pain when eating food		✓	
Myelosuppression (a large decrease in the production of blood cells and platelets by the bone marrow): bleeding, bruising, chills, fatigue, fever, infections, weakness, shortness of breath, or other signs of infection		✓	
Gastrointestinal problems: stomach pain, decreased appetite, diarrhea, nausea, vomiting, vomiting of blood, black stools, constipation, heartburn, swelling or bloating of the abdomen, blood in stool		✓	
Hyperuricemia (high uric acid levels in the blood): joint stiffness or pain, redness,		✓	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
swelling, or difficulty moving your joints			
Sepsis and septic shock (infection of the blood): fever, dizziness, chills, high or very low body temperature, little or no urine, low blood pressure, palpitations, rapid breathing, or rapid heartbeat		✓	
Allergic reaction: difficulty swallowing or breathing, wheezing, drop in blood pressure, feeling sick to your stomach and throwing up, hives, rashes, swelling of the face, lips, tongue or throat		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

IDAMYCIN PFS should be stored at 2°C to 8°C. Protect from light. Discard unused portion.

Keep out of reach and sight of children.

If you want more information about IDAMYCIN PFS:

- Talk to your healthcare professional
- Find the full Product Monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website www.pfizer.ca, or by calling 1-800-463-6001.

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