HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use IDAMYCIN PFS safely and effectively. See full prescribing information for IDAMYCIN PFS.

IDAMYCIN PFS® (idarubicin hydrochloride) injection, for intravenous use
Initial U.S. Approval: 1997

WARNING: CARDIOMYOPATHY, SECONDARY MALIGNANCIES, and EXTRAVASATION AND TISSUE NECROSIS

See full prescribing information for complete boxed warning.

- **Cardiomyopathy: Myocardial damage leading to congestive heart failure can occur with IDAMYCIN PFS. Assess left ventricular cardiac function prior to initiation of IDAMYCIN PFS and during and after treatment. (5.1)**
- **Secondary Malignancies: Secondary acute myelogenous leukemia (AML) and myelodysplastic syndrome (MDS) occur at a higher incidence in patients treated with anthracyclines, including IDAMYCIN PFS. (5.2)**
- **Extravasation of IDAMYCIN PFS during administration can result in local tissue injury and necrosis. Immediately discontinue the IDAMYCIN PFS infusion if extravasation occurs. (2.6, 5.3)**

----------RECENT MAJOR CHANGES----------

Boxed Warning	02/2026
Indications and Usage (1)	02/2026
Dosage and Administration (2)	02/2026
Warnings and Precautions (5)	02/2026

---------- INDICATIONS AND USAGE----------
IDAMYCIN PFS is an anthracycline topoisomerase inhibitor indicated for the treatment of adult patients with acute myeloid leukemia (AML) as a component of a combination chemotherapy regimen. (1)

----------DOSAGE AND ADMINISTRATION----------
Induction Therapy
- 12 mg/m^2 intravenously over 10 to 15 minutes on days 1, 2, and 3 of induction in combination with cytarabine 100 mg/m^2 by continuous intravenous infusion daily for 7 days or cytarabine 25 mg/m^2 intravenous bolus followed by cytarabine 200 mg/m^2 continuous intravenous infusion daily for 5 days. (2.1)
- IDAMYCIN PFS can be given as part of a combination regimen with other chemotherapeutic drugs. (2.1)
- Renal Impairment: Assess renal function prior to therapy. Reduce dosage in renal impairment. (2.3, 8.6)
- Hepatic Impairment: Assess hepatic function prior to therapy. Avoid or reduce dosage in hepatic impairment. (2.4, 8.7)

See full prescribing information for preparation and administration instructions. (2.5, 2.6)

---------- DOSAGE FORMS AND STRENGTHS----------
Injection: 5 mg/5 mL (1 mg/mL), 10 mg/10 mL (1 mg/mL), and 20 mg/20 mL (1 mg/mL) solution in a single-dose vial. (3)

---------- CONTRAINDICATIONS ----------
None. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Myelosuppression: Severe myelosuppression resulting in severe infection, septic shock, hemorrhage, or death may occur. Obtain complete blood counts prior to each treatment and closely monitor patients during treatment for possible clinical complications due to myelosuppression. (5.4)
- Tumor Lysis Syndrome: During treatment, monitor blood chemistries and manage promptly. Treat as clinically indicated. (5.5)
- Hypersensitivity: Monitor patients for hypersensitivity reactions and manage as clinically indicated. (5.6)
- Renal Impairment: Assess renal function prior to and during treatment. Reduce the dose in patients on dialysis or those with GFR <30 mL/min. (2.3, 5.7, 8.6)
- Hepatic Impairment: Obtain liver tests prior to and during therapy. Reduce dose in patients with serum bilirubin levels of 2.6 to 5 mg/dL. Avoid use in patients with serum bilirubin greater than 5 mg/dL. (2.4, 5.8, 8.7)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and to use effective contraception. (5.9, 8.1, 8.3)

---------- ADVERSE REACTIONS ----------
Most common adverse reactions (≥30%) are infection, nausea/vomiting, alopecia, abdominal pain/diarrhea, hemorrhage, mucositis, dermatologic, mental status changes, and pulmonary disorders. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer at 1-800-438-1985 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- USE IN SPECIFIC POPULATIONS ----------
- Lactation: Advise not to breastfeed. (8.2)
- Infertility: May impair fertility. (8.3)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 02/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: CARDIOMYOPATHY, SECONDARY MALIGNANCIES, and EXTRAVASATION AND TISSUE NECROSIS

- **Cardiomyopathy: IDAMYCIN PFS can cause myocardial damage, including acute left ventricular failure, during or after termination of therapy. The risk of cardiomyopathy is increased in patients who have received prior anthracyclines or who have pre-existing cardiac disease. Assess left ventricular cardiac function prior to initiation of IDAMYCIN PFS and during and after treatment *[see Warnings and Precautions (5.1)]*.**
- **Secondary Malignancies: Secondary acute myelogenous leukemia (AML) and myelodysplastic syndrome (MDS) occur at a higher incidence in patients treated with anthracyclines, including IDAMYCIN PFS *[see Warnings and Precautions (5.2)]*.**
- **Extravasation and Tissue Necrosis: Extravasation of IDAMYCIN PFS during administration can result in local tissue injury and necrosis. Immediately terminate the infusion of IDAMYCIN PFS and institute the recommended management procedures *[see Dosage and Administration (2.6) and Warnings and Precautions (5.3)]*.**

1 INDICATIONS AND USAGE

IDAMYCIN PFS is indicated for the treatment of adult patients with acute myeloid leukemia (AML) as a component of a combination chemotherapy regimen.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

Administer IDAMYCIN PFS 12 mg/m^2 intravenously over 10 to 15 minutes on days 1, 2, and 3 of induction in combination with cytarabine. The cytarabine may be given as 100 mg/m^2 by continuous intravenous infusion daily for 7 days or as cytarabine 25 mg/m^2 intravenous bolus followed by cytarabine 200 mg/m^2 continuous intravenous infusion daily for 5 days.

If a response is not achieved with the first induction cycle, a second induction cycle may be administered. Other dosage regimens may be used for a second induction cycle.

Individualize the dose and dosing schedule of IDAMYCIN PFS based on the specific regimen administered, disease state, response to treatment, and patient risk factors.

2.2 Dosage Modifications for Adverse Reactions

Cardiomyopathy

Discontinue IDAMYCIN PFS in patients who develop signs or symptoms of cardiomyopathy *[see Warnings and Precautions (5.1)]*.

Myelosuppression

If patients develop severe myelosuppression, reduce the dose of IDAMYCIN PFS by 25% or as clinically indicated in subsequent cycles *[see Warnings and Precautions (5.4)]*.

Mucositis

If patients develop severe mucositis with IDAMYCIN PFS, reduce the dose by 25% in subsequent cycles. If a second cycle is planned, delay administration in patients who develop severe mucositis until this adverse reaction has resolved *[see Adverse Reactions (6.1)]*.

2.3 Recommended IDAMYCIN PFS Dosage in Patients with Renal Impairment

In patients with renal impairment, reduce the dose of IDAMYCIN PFS as described in Table 1 *[see Use in Specific Populations (8.6)]*.

Table 1: Recommended IDAMYCIN PFS Dosage for Patients with Renal Impairment

Renal Impairment/Estimated GFR	Dosage Modification
GFR greater than or equal to 30 mL/min	No adjustment needed
GFR less than 30 mL/min	Reduce the dose by 33%
Hemodialysis	Reduce the dose by 33%

2.4 Recommended IDAMYCIN PFS Dosage in Patients with Hepatic Impairment

In patients with hepatic impairment, reduce the dose of IDAMYCIN PFS as described in Table 2 *[see Use in Specific Populations (8.7)]*.

Table 2: Recommended IDAMYCIN PFS Dosage for Patients with Hepatic Impairment

Serum Bilirubin	Dosage
Less than or equal to 2.6 mg/dL	No adjustment needed
Greater than 2.6 mg/dL and less than 5 mg/dL	Reduce the dose by 50%
Greater than 5 mg/dL	Avoid Use

2.5 Preparation

- IDAMYCIN PFS is a hazardous drug. Follow applicable special handling and disposal procedures.[1]
- Do not mix IDAMYCIN PFS or administer as an infusion with other drugs or heparin.
- Avoid prolonged contact with any solution of an alkaline pH, as this will result in degradation of IDAMYCIN PFS.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.
- Withdraw the volume of IDAMYCIN PFS needed based on the required dose.
- **Do not** further dilute prior to administration (see section 2.6 Administration).
- Discard unused portion.

2.6 Administration

- IDAMYCIN PFS is for intravenous infusion only.
- Prior to administration, flush the intravenous catheter used for IDAMYCIN PFS administration to ensure patency and to minimize the risk of extravasation.
- Administer IDAMYCIN PFS over 10 to 15 minutes into the tubing of a freely running intravenous infusion of 0.9% Sodium Chloride Injection or 5% Dextrose Injection.
- Closely monitor the infusion site for extravasation or drug infiltration during administration. Manage cases of extravasation as per institutional guidelines.
- Immediately discontinue the infusion if extravasation occurs *[see Warnings and Precautions (5.3)]*.

3 DOSAGE FORMS AND STRENGTHS

Injection: 5 mg/5 mL (1 mg/mL), 10 mg/10 mL (1 mg/mL), and 20 mg/20 mL (1 mg/mL) of idarubicin hydrochloride as a clear, orange-red, preservative-free aqueous solution in a single-dose vial.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Cardiomyopathy

IDAMYCIN PFS can cause myocardial damage, including left ventricular failure, or congestive heart failure (CHF). In pediatric patients, anthracycline-induced cardiomyopathy included impaired left ventricular systolic performance, reduced contractility, congestive heart failure, or death. Cardiomyopathy may develop during treatment with IDAMYCIN PFS or up to several years after completion of treatment. Cases of pericarditis and myocarditis have also been reported at a lower incidence and may not be dose related.

The risk of cardiomyopathy is generally proportional to the cumulative exposure to anthracycline drugs. Include prior doses of other anthracyclines or anthracenediones in calculations of total cumulative dosage for idarubicin hydrochloride. In adult patients, at cumulative doses exceeding 90 mg/m^2 of idarubicin hydrochloride, there is an increased incidence of drug-induced congestive heart failure. The tolerable limit may be lower in patients who received radiation therapy to the mediastinum. Concomitant use of cardiotoxic drugs may increase the risk of idarubicin-induced cardiac toxicity or may result in cardiotoxicity at a lower cumulative anthracycline dose.

Calculate the lifetime cumulative anthracycline exposure prior to each cycle of IDAMYCIN PFS. IDAMYCIN PFS use is not recommended in patients whose lifetime anthracycline exposure has reached the maximum cumulative limit.

Assess left ventricular cardiac function (e.g., MUGA or echocardiogram) prior to initiation of IDAMYCIN PFS. Perform serial cardiac monitoring, which may include electrocardiograms and/or determination of systolic ejection fraction, in all patients during treatment to detect acute changes and after treatment to detect delayed cardiotoxicity. Increase the frequency of assessments as the cumulative anthracycline dose increases or in patients with risk factors for cardiac toxicity. Consider long-term periodic evaluation of cardiac function in these patients.

Adults 65 years of age and older, or with pre-existing cardiac disease, may have an increased risk of anthracycline-induced cardiac toxicity, or may experience cardiotoxicity at a lower cumulative anthracycline dose.

Discontinue IDAMYCIN PFS in patients who develop signs or symptoms of cardiomyopathy.

5.2 Secondary Malignancies

The risk of developing secondary AML and myelodysplastic syndrome (MDS) is increased following treatment with IDAMYCIN PFS. AML and MDS have occurred in patients treated with anthracycline topoisomerase inhibitors when used in combination with other antineoplastic agents or radiation therapy. Monitor patients long-term for the development of secondary malignancies.

5.3 Severe Local Tissue Necrosis with Extravasation

Extravasation of IDAMYCIN PFS at the site of intravenous administration can cause severe local tissue injury including blistering, ulceration, thrombophlebitis, and necrosis requiring wide excision of the affected area and skin grafting.

Monitor patients during the IDAMYCIN PFS infusion for signs and symptoms of extravasation (including erythematous streaking, burning, or stinging sensations, thrombosis) or perivenous infiltration.

If extravasation occurs during administration, immediately discontinue the intravenous injection or continuous intravenous infusion of IDAMYCIN PFS and manage per institutional guidelines *[see Dosage and Administrations (2.6)]*.

5.4 Severe Myelosuppression

Severe myelosuppression resulting in severe infection, septic shock, hemorrhage, or death may occur during treatment with IDAMYCIN PFS, and some patients may require blood product transfusions.

Obtain complete blood counts prior to each treatment and closely monitor patients during treatment for possible clinical complications due to myelosuppression. Delay next dose of IDAMYCIN PFS if severe myelosuppression has not improved. Consider dose reduction for patients with prolonged myelosuppression *[see Dosage and Administrations (2.2)]*.

Discontinue IDAMYCIN PFS in patients who develop severe myelosuppression.

5.5 Tumor Lysis Syndrome

IDAMYCIN PFS may induce tumor lysis syndrome. Patients at risk of tumor lysis syndrome are those with rapidly growing tumors or high tumor burden prior to treatment.

During and after initial treatment, monitor blood chemistries and manage abnormalities promptly. Hydration, urine alkalinization, and prophylaxis with allopurinol to prevent hyperuricemia may minimize potential complications of tumor lysis syndrome.

5.6 Hypersensitivity

IDAMYCIN PFS can cause hypersensitivity reactions.

Clinical signs and symptoms of hypersensitivity may include, but are not limited to, rash and urticaria *[see Adverse Reactions (6.1)]*. Monitor patients for signs and symptoms of hypersensitivity during treatment with IDAMYCIN PFS and manage as clinically indicated.

5.7 Use in Patients with Renal Impairment

Renal impairment may result in increased risk of toxicity in patients treated with IDAMYCIN PFS *[see Use in Specific Populations (8.6)]*.

Assess renal function prior to and during treatment with IDAMYCIN PFS.

Reduce the dose of IDAMYCIN PFS in patients on dialysis or those with GFR <30 mL/min *[see Dosage and Administration (2.3)]*.

5.8 Use in Patients with Hepatic Impairment

Hepatic impairment may result in increased risk of toxicity in patients treated with IDAMYCIN PFS *[see Use in Specific Populations (8.7)]*.

Obtain liver tests including ALT, AST, alkaline phosphatase, and bilirubin prior to and during therapy.

Reduce the dose of IDAMYCIN PFS in patients with serum bilirubin levels of 2.6 to 5 mg/dL. Avoid use of IDAMYCIN PFS in patients with serum bilirubin greater than 5 mg/dL *[see Dosage and Administration (2.4)]*.

5.9 Embryo-Fetal Toxicity

Based on findings from animal reproductive studies and its mechanism of action *[see Clinical Pharmacology (12.1)]*, IDAMYCIN PFS can cause fetal harm when administered to pregnant women. Idarubicin hydrochloride was embryotoxic and teratogenic in rats at doses of 1.2 mg/m^2/day or 0.1 times the human dose, which was not maternally toxic. Idarubicin hydrochloride was embryotoxic but not teratogenic in rabbits at doses of 2.4 mg/m^2/day or 0.2 times the human dose, which was maternally toxic. Advise women of the potential risk to the fetus.

Advise females of reproductive potential to use effective contraception during treatment with IDAMYCIN PFS and for 6.5 months after the last dose. Advise males with female partners of reproductive potential to use effective contraception for 3.5 months after the last dose *[see Use in Specific Populations (8.1, 8.3) and Nonclinical Toxicology (13.1)]*.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Cardiomyopathy *[see Warnings and Precautions (5.1)]*
- Secondary Malignancies *[see Warnings and Precautions (5.2)]*
- Severe Local Tissue Necrosis with Extravasation *[see Warnings and Precautions (5.3)]*
- Severe Myelosuppression *[see Warnings and Precautions (5.4)]*
- Tumor Lysis Syndrome *[see Warnings and Precautions (5.5)]*
- Hypersensitivity *[see Warnings and Precautions (5.6)]*

6.1 Clinical Trials and Postmarketing Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of IDAMYCIN PFS in combination with cytarabine has been evaluated in four controlled clinical studies with 823 patients with AML randomized to receive idarubicin hydrochloride (n=401) or daunorubicin (n=422) *[see Clinical Studies (14)]*.

Southeastern Cancer Study Group (SEG)

Table 3 below lists the adverse reactions that occurred in patients with AML who received idarubicin hydrochloride in the Southeastern Cancer Study Group (SEG) study.

Table 3: Adverse Reactions (≥5%) in Patients with AML Who Received Idarubicin Hydrochloride as Induction Therapy in the SEG Trial

Adverse Reactions	Idarubicin with Cytarabine (N=110)	Daunorubicin with Cytarabine (N=118)
	All Grades %	All Grades %
Infection	95	97
Nausea/Vomiting	82	80
Alopecia	77	72
Abdominal Pain/Diarrhea	73	68
Hemorrhage	63	65
Mucositis	50	55
Dermatologic	46	40
Mental Status Changes	41	34

Pulmonary Disorders	39	39
Fever	26	28
Headache	20	24
Cardiac Disorder	16	24
Peripheral Neuropathy	7	9

Clinically relevant adverse reactions in <5% of patients who received idarubicin hydrochloride included pulmonary allergy, seizure, and cerebellar adverse reactions.

Other Clinical Trials

The following additional adverse reactions associated with the use of idarubicin hydrochloride were identified in clinical studies or postmarketing reports. Because some of these reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Cardiac

- Asymptomatic declines in Left Ventricular Ejection Fraction (LVEF)
- Chest pain
- Congestive heart failure
- Myocardial infarction
- Serious arrhythmias including atrial fibrillation

Dermatologic

- Bullous erythrodermatous rash (palms and soles)
- Generalized rash
- Radiation recall (skin reaction)
- Urticaria

Gastrointestinal

- Severe enterocolitis with perforation

Hepatic

- Increased ALT/AST

Renal

- Renal impairment

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on findings from animal reproduction studies and its mechanism of action, IDAMYCIN PFS can cause fetal harm when administered to a pregnant woman *[see Warnings and Precautions (5.9)]*. There are no available data on the use of IDAMYCIN PFS in pregnant women to evaluate for a drug-associated risk.

Idarubicin hydrochloride was embryotoxic and teratogenic in rats at doses of 1.2 mg/m^2/day or 0.1 times the human dose. Idarubicin hydrochloride was embryotoxic but not teratogenic in rabbits at doses of 2.4 mg/m^2/day or 0.2 times the human dose *[see Data]*. Advise women of the potential risk to the fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

Idarubicin hydrochloride was embryotoxic and teratogenic in the rat at a dose of 1.2 mg/m^2/day or 0.1 times the human dose, which was not maternally toxic. Idarubicin hydrochloride was embryotoxic but not teratogenic in the rabbit even at a dose of 2.4 mg/m^2/day or 0.2 times the human dose, which was maternally toxic.

8.2 Lactation

Risk Summary

There are no data on the presence of idarubicin hydrochloride or its metabolites in human milk, the effects on the breastfed child or the effects on milk production. Because of the potential for serious adverse reactions in the breastfed child, including myelosuppression, cardiac toxicity and malignancy, advise women not to breastfeed during treatment with IDAMYCIN PFS and for 14 days after the last dose.

8.3 Females and Males of Reproductive Potential

Based on mechanism of action and findings in animals, IDAMYCIN PFS can cause fetal harm *[see Use in Specific Populations (8.1)]*.

Pregnancy Testing

Verify the pregnancy status of female patients of reproductive potential prior to initiating therapy with IDAMYCIN PFS.

Contraception

Females

Advise females of reproductive potential to use effective contraception during treatment with IDAMYCIN PFS and for 6.5 months after the last dose.

Males

Based on the genotoxicity potential, advise males with female partners of reproductive potential to use effective contraception during treatment with IDAMYCIN PFS and for 3.5 months after the last dose.

Infertility

Based on animal studies and mechanism of action, IDAMYCIN PFS may impair fertility in males and females of reproductive potential *[see Nonclinical Toxicology (13.1)]*. It is not known if these effects are reversible.

8.4 Pediatric Use

The safety and effectiveness of IDAMYCIN PFS in pediatric patients have not been established. Pediatric patients may be at greater risk for anthracycline-induced acute manifestations of cardiotoxicity or late cardiovascular dysfunction.

The safety and effectiveness of idarubicin hydrochloride were assessed but not established in two open label clinical studies in pediatric patients aged 1 to <17 years with leukemia and solid tumors. The pharmacokinetics of idarubicin hydrochloride in these pediatric patients were within range of that observed in adult patients given a similar dose based on body surface area.

Idarubicin hydrochloride and idarubicinol were detected in CSF samples obtained in these patients; the clinical relevance of these findings is unknown.

8.5 Geriatric Use

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 Adverse Reactions (6.1)]*.

8.6 Renal Impairment

Reduce dosage of IDAMYCIN PFS in patients with GFR less than 30 mL/min and in patients on hemodialysis *[see Dosage and Administration (2.3)]*. Renal function should be evaluated prior to and during treatment with IDAMYCIN PFS.

The effect of renal impairment on idarubicin hydrochloride or idarubicinol pharmacokinetics is unknown *[see Clinical Pharmacology (12.3)]*. However, renal impairment can affect the disposition of idarubicin hydrochloride based on a mechanistic understanding of idarubicin hydrochloride elimination. Treatment was not given if creatinine serum levels exceeded 2 mg/dL in multiple clinical trials.

8.7 Hepatic Impairment

Reduce dosage of IDAMYCIN PFS in patients with serum bilirubin levels greater than 2.6 mg/dL and less than 5 mg/dL *[see Dosage and Administration (2.4)]*. Do not administer IDAMYICN PFS in patients with serum bilirubin levels greater than 5 mg/dL. Liver function should be evaluated prior to and during treatment with IDAMYCIN PFS.

The effect of hepatic impairment on idarubicin hydrochloride or idarubicinol pharmacokinetics is unknown *[see Clinical Pharmacology (12.3)]*. However, hepatic impairment can affect the disposition of idarubicin hydrochloride based on a mechanistic understanding of idarubicin hydrochloride elimination.

10 OVERDOSAGE

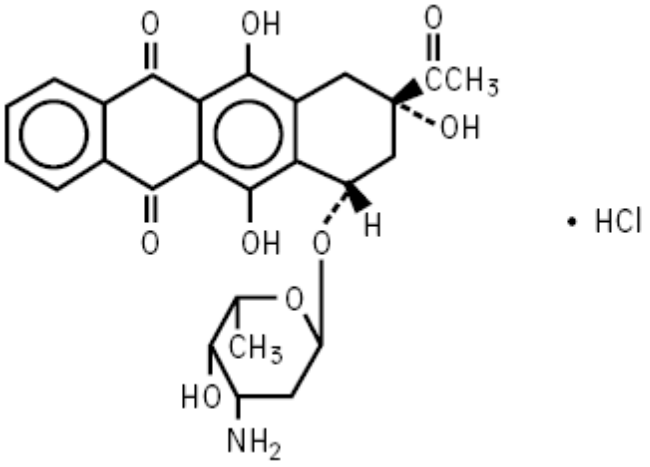
There is no known antidote to idarubicin hydrochloride. Two cases of fatal overdosage in patients receiving therapy for AML have been reported. The doses were 135 mg/m^2 over 3 days and 45 mg/m^2 of idarubicin hydrochloride and 90 mg/m^2 of daunorubicin over a three-day period.

Based on multicompartment and extravascular distribution, tissue binding, and low unbound fraction available in plasma, hemodialysis or peritoneal dialysis are unlikely to significantly reduce exposure during an overdosage.

11 DESCRIPTION

IDAMYCIN PFS contains idarubicin hydrochloride, which is an anthracycline topoisomerase inhibitor.

Chemically, idarubicin hydrochloride is 5, 12-Naphthacenedione, 9-acetyl-7-[(3-amino-2,3,6-trideoxy-α-L-*lyxo*-hexopyranosyl)oxy]-7,8,9,10-tetrahydro-6,9,11-trihydroxyhydrochloride, (7S-*cis*). The structural formula is as follows:



$C_{26}H_{27}NO_9 \cdot HCl$ M.W. 533.96

IDAMYCIN PFS injection, for intravenous use, is a sterile, orange-red, isotonic parenteral preservative-free solution, available in 5 mL (5 mg), 10 mL (10 mg), and 20 mL (20 mg) single-dose only vials.

Each mL contains idarubicin hydrochloride, USP 1 mg (equivalent to 0.93 mg idarubicin free base) and the following inactive ingredients: Glycerin, USP 25 mg and Water for Injection, USP q.s. Hydrochloric Acid, NF is used to adjust the pH to a target of 3.5.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Idarubicin hydrochloride has antimitotic and cytotoxic activity through forming complexes with the DNA, inhibiting nucleic acid synthesis, inhibiting topoisomerase II activity, and producing DNA-damaging free radicals.

12.2 Pharmacodynamics

Idarubicin hydrochloride exposure-response relationships and the time course of pharmacodynamic response have not been fully characterized.

12.3 Pharmacokinetics

Idarubicin hydrochloride pharmacokinetics were determined in adult leukemia patients with normal renal and hepatic function following intravenous administration of idarubicin hydrochloride 10 to 12 mg/m^2 daily for 3 to 4 days as a single agent or combined with cytarabine.

Accumulation is predicted to be 1.7-fold for idarubicin hydrochloride and 2.3-fold for idarubicinol following multiple idarubicin hydrochloride dosing.

Distribution

Idarubicin hydrochloride exhibits a rapid distributive phase with a very large volume of distribution. Idarubicin hydrochloride is approximately 97% and idarubicinol is 94% bound to plasma proteins and the binding is concentration independent.

Concentrations of idarubicin hydrochloride and idarubicinol in nucleated blood and bone marrow cells are more than a hundred times the plasma concentrations.

Elimination

Idarubicin hydrochloride mean (range) terminal half-life is 22 (4 to 48) hours when used as a single agent and 20 (7 to 38) hours when used in combination with cytarabine. Idarubicin hydrochloride plasma clearance is twice the expected hepatic plasma flow.

Idarubicinol mean terminal half-life exceeds 45 hours; hence, its plasma levels are sustained for a period greater than 8 days.

Metabolism

The idarubicin hydrochloride is primary metabolized to the active metabolite idarubicinol which has cytotoxic activity that likely contributes to the effects of idarubicin hydrochloride.

Excretion

Idarubicin hydrochloride is eliminated predominately by biliary excretion and to a lesser extent by renal excretion, primarily as idarubicinol.

Specific Populations

The effect of renal or hepatic impairment on idarubicin hydrochloride or idarubicinol pharmacokinetics is unknown.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies have not been conducted with idarubicin hydrochloride. Idarubicin hydrochloride and related compounds have been shown to have mutagenic and carcinogenic properties when tested in experimental models (including bacterial systems, mammalian cells in culture and female Sprague Dawley rats).

In male dogs given 1.8 mg/m^2/day 3 times/week (about one seventh the weekly human dose on a mg/m^2 basis) for 13 weeks, or 3 times the human dose, testicular atrophy was observed with inhibition of spermatogenesis and sperm maturation with few or no mature sperm. These effects were not readily reversed after a recovery of 8 weeks.

14 CLINICAL STUDIES

The efficacy of IDAMYCIN PFS was evaluated in four randomized, controlled clinical studies (Memorial Sloan Kettering Cancer Center (MSKCC), Southeastern Cancer Study Group (SEG), US Multicenter, and Gruppo Italiano Malattie Ematologiche Maligne dell'Adulto (GIMEMA) trials) of 823 adult patients with newly-diagnosed AML. Patients were randomized to receive either idarubicin hydrochloride (IDR) or daunorubicin (DNR) in combination with cytarabine (Ara C) as induction therapy. Median age for IDR versus DNR in the MSKCC, SEG, US Multicenter, and GIMEMA studies was 36 versus 41, 60 versus 61, 56 versus 55, and 63 versus 62 years, respectively. Incidence of male sex was 45% versus 46%, 53% versus 47%, 57% versus 56%, and 52% versus 59%, respectively.

Idarubicin hydrochloride was administered as an induction regimen of 12 mg/m^2 (or 13 mg/m^2 [1.1 times the recommended dosage] in US Multicenter study only) once a day for 3 days in combination with cytarabine. Daunorubicin was administered as an induction regimen of 45 mg/m^2 (or 50 mg/m^2 in MSKCC study only) daily for 2 days. Cytarabine was administered 100 mg/m^2 daily by continuous infusion for 7 days or as 25 mg/m^2 intravenous bolus followed by 200 mg/m^2 daily for 5 days continuous infusion (MSKCC only). Patients who had persistent leukemia after the first induction course could receive a second course of induction therapy.

Patients received the same anthracycline for consolidation as was used for induction, in combination with cytarabine (and 6-thioguanine for the SEG study only). The SEG study also included maintenance therapy with the same anthracycline used in induction in combination with

cytarabine. The efficacy or safety have not been established for IDAMYCIN PFS for use as consolidation or maintenance therapy. Efficacy results for the four trials are provided in Table 4.

Table 4: Efficacy Results in Patients with AML in MSKCC, SEG, US Multicenter, and GIMEMA Studies[X]

	MSKCC		SEG		US Multicenter		GIMEMA	
	IDR + Ara C	DNR + Ara C	IDR + Ara C	DNR + Ara C	IDR + Ara C	DNR + Ara C	IDR + Ara C	DNR + Ara C
Complete Remission Rate n/N (%)	51/65* (78%)	38/65 (58%)	76/111* (68%)	65/119 (55%)	68/101 (67%)	66/113 (58%)	49/124 (40%)	49/125 (39%)
Median Overall Survival (months)	16.7*	14.3	10.8	9.1	12.9*	9.2	2.9	5.6

[X] All randomized patients

* Overall $p < 0.05$, unadjusted for prognostic factors or multiple endpoints

15 REFERENCES

1. "OSHA Hazardous Drugs." OSHA. http://www.osha.gov/SLTC/hazardousdrugs/index.html.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

IDAMYCIN PFS (idarubicin hydrochloride) injection is a clear, orange-red, aqueous, preservative-free solution available as follows:

Single-dose Cytosafe™ vials:

Unit of Sale	Concentration
NDC 0013-2576-91 Carton of 1 Single-dose Vial	5 mg/5 mL (1 mg/mL)
NDC 0013-2586-91 Carton of 1 Single-dose Vial	10 mg/10 mL (1 mg/mL)
NDC 0013-2596-91 Carton of 1 Single-dose Vial	20 mg/20 mL (1 mg/mL)

Single-dose glass vials:

Unit of Sale	Concentration
NDC 0013-2576-05 Carton of 1 Single-dose Vial	5 mg/5 mL (1 mg/mL)
NDC 0013-2586-10 Carton of 1 Single-dose Vial	10 mg/10 mL (1 mg/mL)
NDC 0013-2596-20 Carton of 1 Single-dose Vial	20 mg/20 mL (1 mg/mL)

Storage and Handling

Store refrigerated at 2ºC to 8ºC (36ºF to 46ºF). Store and dispense in the original carton until time of use to protect from light.

IDAMYCIN PFS is a hazardous drug. Follow applicable special handling and disposal procedures.[1]

17 PATIENT COUNSELING INFORMATION

Cardiomyopathy

Inform patients that IDAMYCIN PFS can cause irreversible myocardial damage. Advise patients to immediately contact their healthcare provider during or after treatment with IDAMYCIN PFS for symptoms of heart failure, including new onset or worsening shortness of breath, cough, swelling of the ankles/legs, swelling of the face, palpitations, weight gain of more than 5 pounds in 24 hours, dizziness, or loss of consciousness *[see Warnings and Precautions (5.1)]*.

Secondary Malignancies

Inform patients that there is an increased risk of secondary malignancies with IDAMYCIN PFS *[see Warnings and Precautions (5.2)]*.

Extravasation and Tissue Necrosis

Inform patients that IDAMYCIN PFS can cause severe injection site reactions. Advise patients to contact a healthcare provider if injection site pain occurs after receiving IDAMYCIN PFS *[see Warnings and Precautions (5.3)]*.

Severe Myelosuppression

Inform patients that IDAMYCIN PFS causes bone marrow suppression at therapeutic doses resulting in an increased risk of infection or hemorrhage. Advise patients to contact their healthcare provider for new onset fever or symptoms of infection or hemorrhage *[see Warnings and Precautions (5.4)]*.

Tumor Lysis Syndrome

Advise patients to contact their healthcare provider promptly to report any signs and symptoms of tumor lysis syndrome (fever, chills, nausea, vomiting, confusion, shortness of breath, seizure, irregular heartbeat, dark or cloudy urine, unusual tiredness, muscle pain, and/or joint discomfort) *[see Warnings and Precautions (5.5)]*.

Alopecia

Inform patients that IDAMYCIN PFS causes alopecia (usually reversible) in most patients *[see Adverse Reactions (6.1)]*.

Red Discoloration of Bodily Fluids

Inform patients that IDAMYCIN PFS may transiently impart a red coloration to bodily fluids, including the urine, after administration.

Gastrointestinal Adverse Reactions

Inform patients that IDAMYCIN PFS can cause nausea, vomiting, diarrhea, and mucositis. Advise patients to contact a healthcare provider if nausea, vomiting, diarrhea, or mucositis occur *[see Adverse Reactions (6.1)]*.

Embryo-Fetal Toxicity

IDAMYCIN PFS can cause fetal harm. Advise females of reproductive potential to inform their healthcare provider of a known or suspected pregnancy *[see Warnings and Precautions (5.9), Use in Specific Populations (8.1, 8.3), and Nonclinical Toxicology (13.1)]*.

Advise female patients of reproductive potential to use effective contraception during treatment with IDAMYCIN PFS and for 6.5 months after the last dose *[see Warnings and Precautions (5.9), Use in Specific Populations (8.1, 8.3), and Nonclinical Toxicology (13.1)]*.

Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3.5 months after the last dose of IDAMYCIN PFS. *[see Warnings and Precautions (5.9), Use in Specific Populations (8.1, 8.3), and Nonclinical Toxicology (13.1)]*.

Lactation

Advise women not to breastfeed during treatment with IDAMYCIN PFS and for 14 days after the last dose *[see Use in Specific Populations (8.2)]*.

Infertility

Advise male and female patients of reproductive potential that IDAMYCIN PFS may impair fertility *[see Use in Specific Populations (8.3) and Nonclinical Toxicology (13.1)]*.

This product's labeling may have been updated. For the most recent prescribing information, please visit www.pfizer.com.

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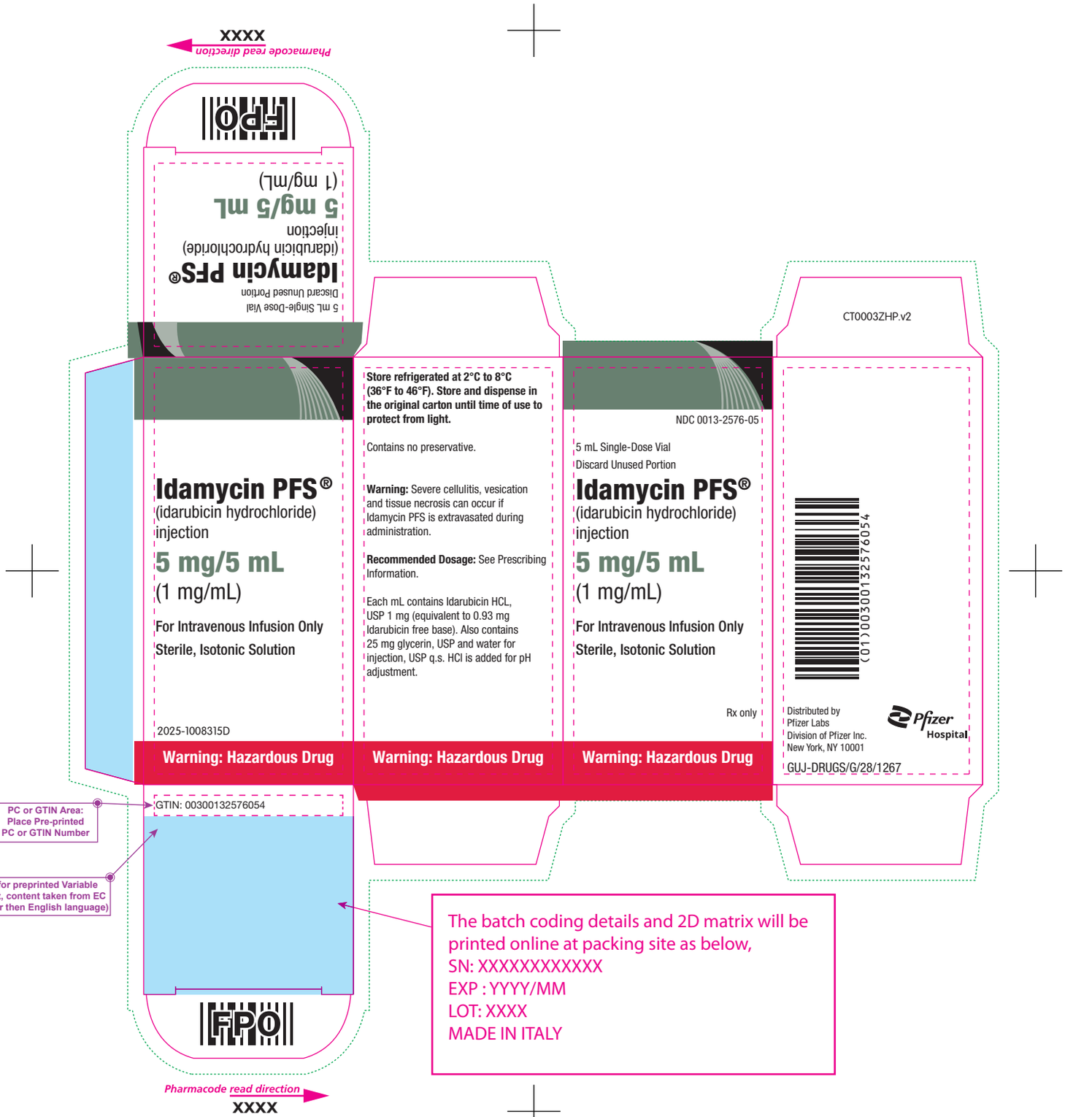
LAB-0131-9.3



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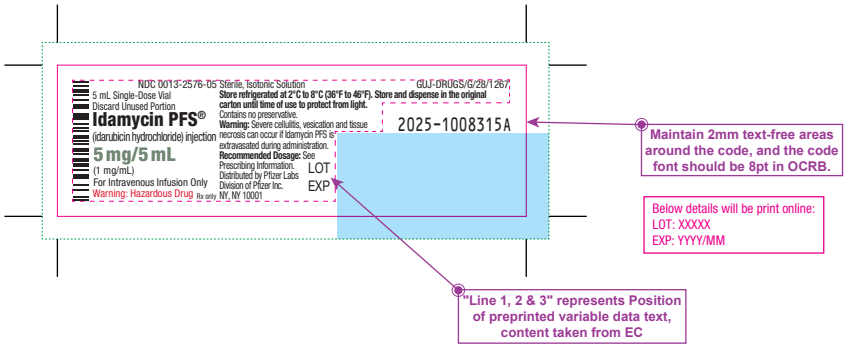

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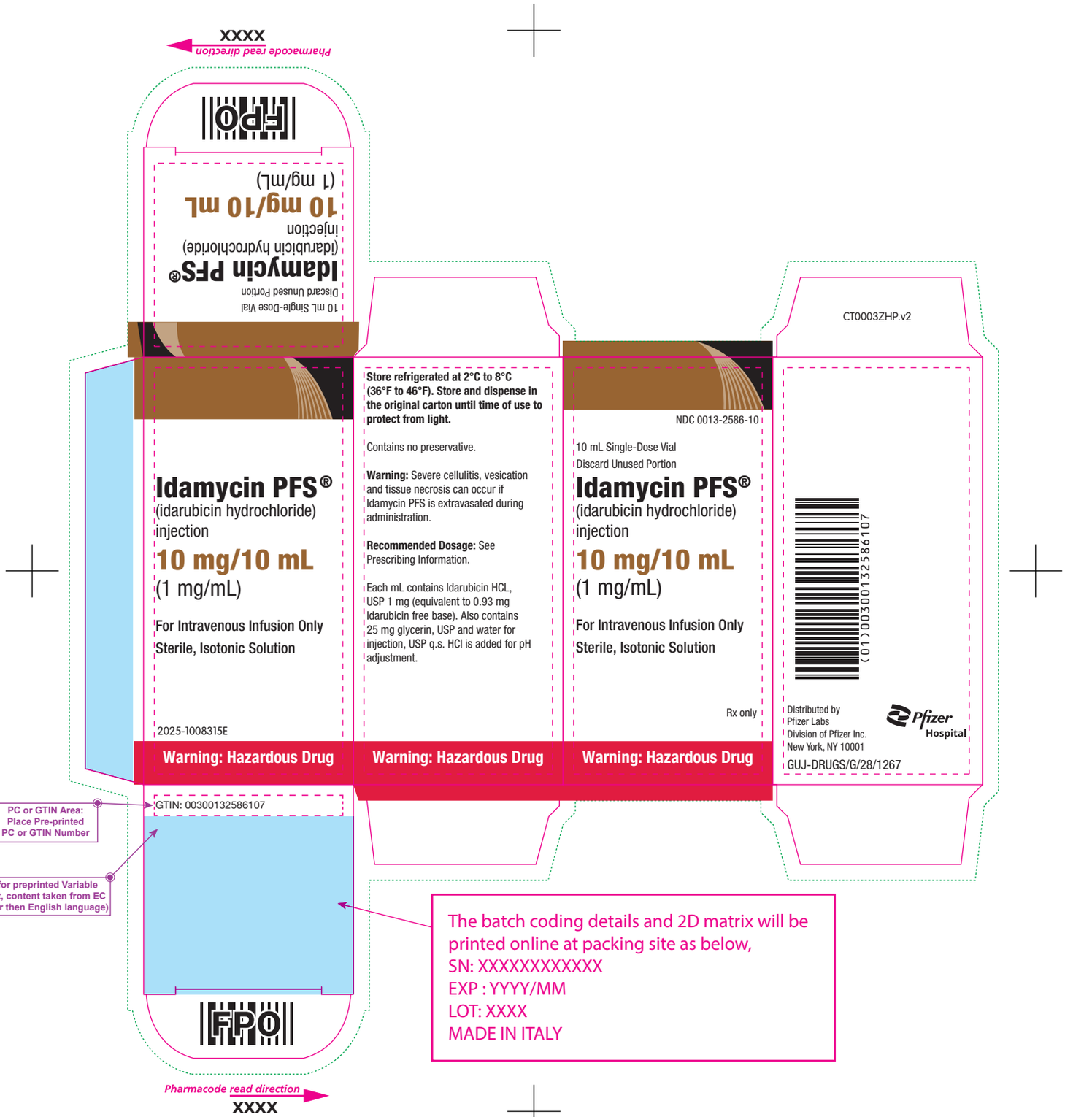

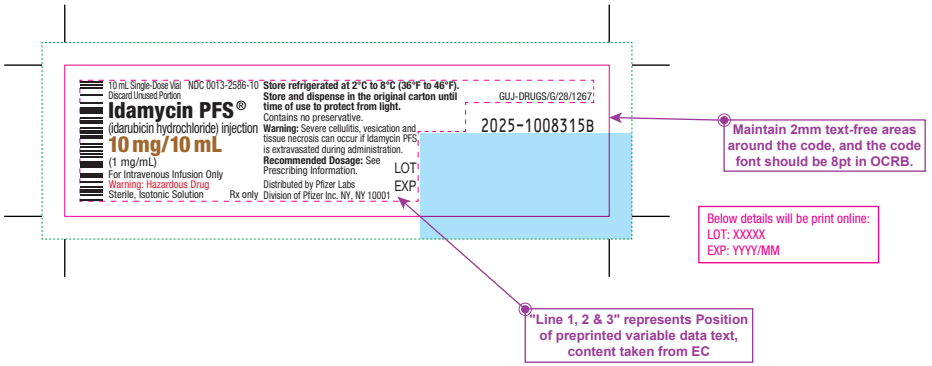

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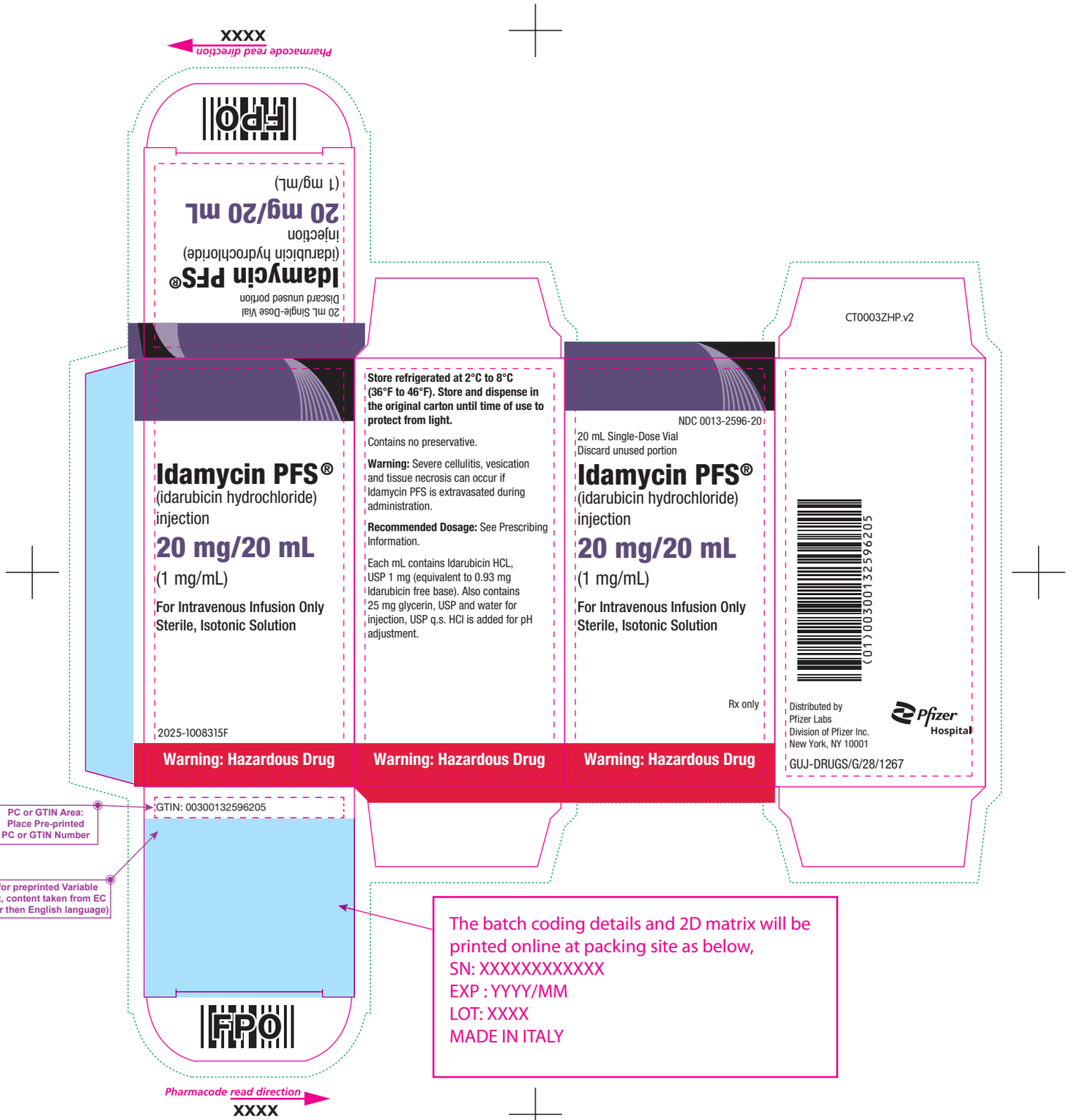

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LOT: XXXX
MADE IN ITALY

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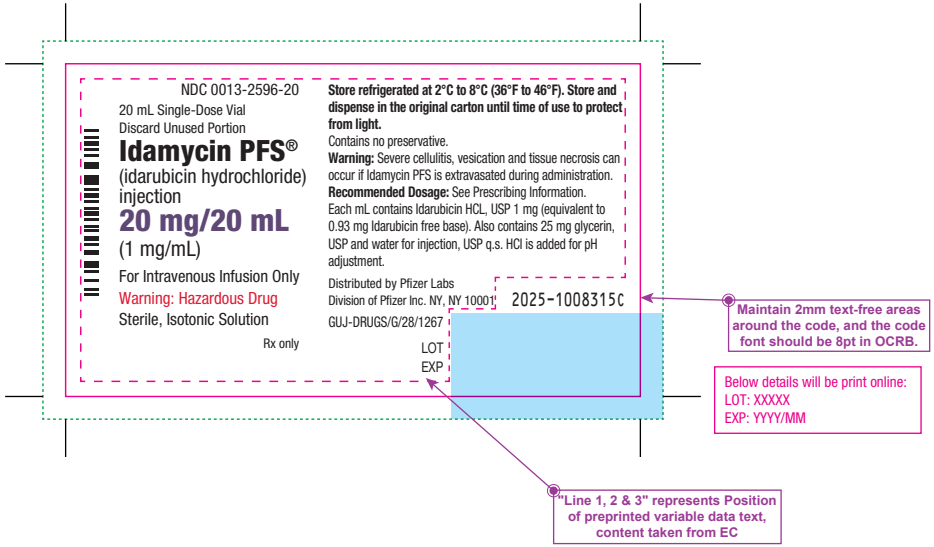

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(b) (4)

Store refrigerated at 2°C to 8°C (36°F to 46°F). Store and dispense in the original carton until time of use to protect from light.

Contains no preservative.

Warning: Severe cellulitis, vesication and tissue necrosis can occur if Idamycin PFS is extravasated during administration.

Recommended Dosage:
See Prescribing Information.

Each mL contains Idarubicin HCL, USP 1 mg (equivalent to 0.93 mg Idarubicin free base). Also contains 25 mg glycerin, USP and water for injection, USP q.s. HCl is added for pH adjustment.

Warning: Hazardous Drug

NDC 0013-2576-91

5 mL Single-Dose CYTOSAFE® Vial
Discard Unused Portion

Idamycin PFS®
(idarubicin hydrochloride)
injection

5 mg/5 mL
(1 mg/mL)

For Intravenous Infusion Only
Sterile, Isotonic Solution

Rx only

Warning: Hazardous Drug

2025-1008359-B
LOT XXXXXXX
EXP YYYY/MM
GTIN 00300132576917
SN

Quiet zone
Quiet zone
2D code area
Quiet zone
Quiet zone

MADE IN AUSTRALIA

3 00132 57691 7

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Pfizer Hospital

Idamycin PFS®
(idarubicin hydrochloride)
injection

5 mg/5 mL
(1 mg/mL)

For Intravenous Infusion Only
Sterile, Isotonic Solution

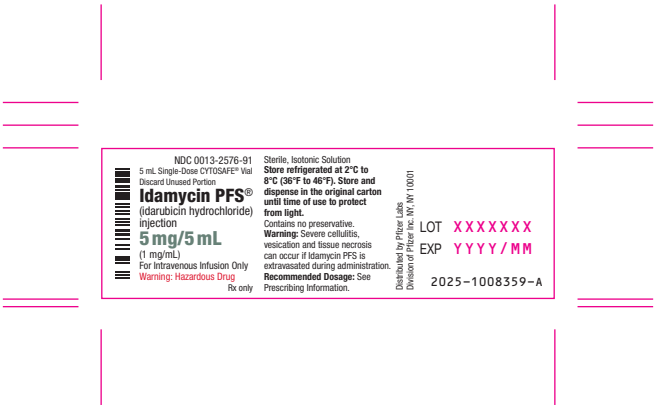
Warning: Hazardous Drug

5 mL Single-Dose CYTOSAFE® Vial

Idamycin PFS®
(idarubicin hydrochloride)
injection

5 mg/5 mL
(1 mg/mL)

(b) (4)



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Store refrigerated at 2°C to 8°C (36°F to 46°F). Store and dispense in the original carton until time of use to protect from light.

Contains no preservative.

Warning: Severe cellulitis, vesication and tissue necrosis can occur if Idamycin PFS is extravasated during administration.

Recommended Dosage:
See Prescribing Information.

Each mL contains Idarubicin HCL, USP 1 mg (equivalent to 0.93 mg Idarubicin free base). Also contains 25 mg glycerin, USP and water for injection, USP q.s. HCl is added for pH adjustment.

Warning: Hazardous Drug

NDC 0013-2586-91

10 mL Single-Dose CYTOSAFE® Vial
Discard Unused Portion

Idamycin PFS®
(idarubicin hydrochloride)
injection

10 mg/10 mL
(1 mg/mL)

For Intravenous Infusion Only
Sterile, Isotonic Solution

Rx only

Warning: Hazardous Drug

2025-1008359-D
LOT XXXXXXX
EXP YYYY/MM
GTIN 00300132586916
SN

Quiet zone
Quiet zone
2D code area
Quiet zone
Quiet zone

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3 00132 58691 6

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Pfizer Hospital

Idamycin PFS®
(idarubicin hydrochloride)
injection

10 mg/10 mL
(1 mg/mL)

For Intravenous Infusion Only
Sterile, Isotonic Solution

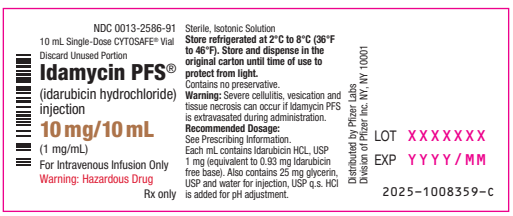
Warning: Hazardous Drug

10 mL Single-Dose CYTOSAFE® Vial

Idamycin PFS®
(idarubicin hydrochloride)
injection

10 mg/10 mL
(1 mg/mL)

(b) (4)



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Store refrigerated at 2°C to 8°C (36°F to 46°F). Store and dispense in the original carton until time of use to protect from light.

Contains no preservative.

Warning: Severe cellulitis, vesication and tissue necrosis can occur if Idamycin PFS is extravasated during administration.

Recommended Dosage:
See Prescribing Information.

Each mL contains Idarubicin HCL, USP 1 mg (equivalent to 0.93 mg Idarubicin free base). Also contains 25 mg glycerin, USP and water for injection, USP q.s. HCl is added for pH adjustment.

Warning: Hazardous Drug

NDC 0013-2596-91

20 mL Single-Dose CYTOSAFE® Vial
Discard Unused Portion

Idamycin PFS®
(idarubicin hydrochloride)
injection

20 mg/20 mL
(1 mg/mL)

For Intravenous Infusion Only
Sterile, Isotonic Solution

Rx only

Warning: Hazardous Drug

2025-1008359-F
LOT XXXXXXX
EXP YYYY/MM
GTIN 00300132596915
SN

Quiet zone
Quiet zone
2D code area
Quiet zone
Quiet zone

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3 00132 59691 5

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Pfizer Hospital

Idamycin PFS®
(idarubicin hydrochloride)
injection

20 mg/20 mL
(1 mg/mL)

For Intravenous Infusion Only
Sterile, Isotonic Solution

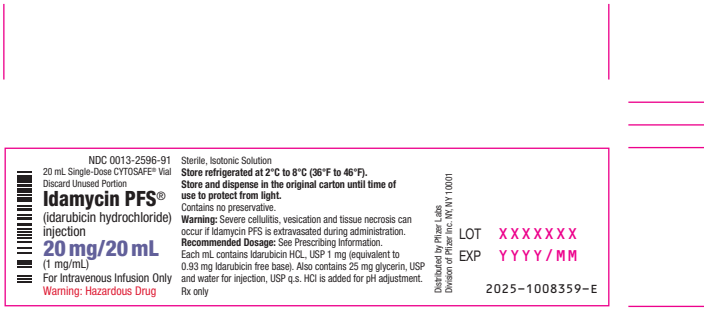
Warning: Hazardous Drug

20 mL Single-Dose CYTOSAFE® Vial

Idamycin PFS®
(idarubicin hydrochloride)
injection

20 mg/20 mL
(1 mg/mL)

(b) (4)



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