health
Department:
Health
REPUBLIC OF SOUTH AFRICA

Private Bag X828, PRETORIA, 0001 Dr AB Xuma Building1112 Voortrekker Road, Pretoria Townlands 351-JR, PRETORIA, 0187 Tel (012) 395 8000, Fax (012) 395 8918

Mr E van Zyl
Equity Pharmaceuticals (Pty) Ltd
100 Sovereign Road
Route 21 Corporate Park
Nellmapius Drive
Irene
Pretoria

Dear Mr van Zyl

Section 21 Authorization for IDARUBICIN 10MG INJECTION

Attached, please find the Authorization for exemption under Section 21 of the Medicines and Related Substances Act by SAHPRA granted for:

- **Idarubicin 10mg Injection**

The quantities for which approval was granted are only estimates based on procurement by provinces over the last 6 months. Please note that the National Department of Health (NDOH) cannot guarantee the procurement of these quantities, as NDOH has no control over orders being placed by provincial depots, and current stock holding might influence estimated quantities.

The following process will be followed to ensure the quality of the product being brought in:

1. Manufacturer will submit an assay and identification of every batch imported.
2. An additional assay of every batch will be done by a quality control laboratory.
3. A random sample will be assayed during the authorized period by a quality control laboratory.
4. Aggregate statistics to be submitted to NDOH in the first week of each month of all orders received and quantities supplied per province.
5. The NDOH needs to be advised of the quantities and date of arrival of stocks in terms of this authorization within 7 days after arrival.
6. The supplier will provide monthly reports, by the 7th of each month, using the attached format of orders received and issues done.
7. Participating Authorities (PAs) will provide a consolidated close out report of usage using the attached format on the date when an authorization lapses.

8. The full quantities imported in terms of this Section 21authorisation must be accounted for.
9. Note that this authorization DOES NOT cover supplies to the private sector.
10. Where this authorization is obtained to provide security of supply due to supply challenges from the contracted supplier, PAs are requested to buy out against contracted suppliers and ensure that related orders are cancelled accordingly to prevent overstocking once the contracted supplier gets back into stock.

It should be noted this authorization applies only for use of the product in the public sector with estimated usage quantities for a period of one month. The authorization is expected to expire on **23 March 2027**.

Table 1: Provincial uptake

Province	Six Months Estimate
Correctional Services	0
EC-MT	0
EC-PE	100
FS	0
GP	80
KZN	150
LP	0
MP	0
NC	0
NW	0
SAMHS	0
WC	30
Total	**360**

Yours sincerely

K Jamaloodien

KHADIJA JAMALOODIEN
CHIEF DIRECTOR: HEALTH PRODUCTS PROCUREMENT
DATE: 28/9/2026

S2100038261

SAHPRA Head Office
Building A, Loftus Park
2nd Floor
Kirkness Street
Arcadia
0083

Section 21 Outcome Letter

2026-09-25

Ms Khadija Jamaloodien

Voortrekker Road, First, Dr AB Xuma, National Department Of Health, Voortrekker Road, Pretoria Townlands 351-Jr, Pretoria, South Africa, Voortrekker Road, Pretoria, Gauteng, Pretoria, Gauteng

Pretoria, Gauteng

buhle.mbongo@health.gov.za

Dear Ms Khadija Jamaloodien

REQUEST TO USE UNREGISTERED MEDICINE IN TERMS OF SECTION 21 OF THE MEDICINES AND CONTROLLED SUBSTANCES ACT, 1965 (ACT 101 of 1965):

Your application dated **2026-09-23** refers

A. STATUS: Approved

B. APPLICANT: Ms Khadija Jamaloodien

C. IMPORTING COMPANY: EQUITY PHARMACEUTICAL (PTY) LTD

D. NUMBER OF PATIENT/(S) INTENDED TO BE TREATED: 1

E. UNREGISTERED MEDICINES: GENERIC NAME (INN / ACTIVE INGREDIENT): Idarub

F. TRADE NAME: Idarub 10 mg

G. QUANTITY: 360 Packs (1)

SAHPRA
South African
Health Products
Regulatory Authority

SAHPRA Head Office
Building A, Loftus Park
2nd Floor
Kirkness Street
Arcadia
0083

H. LETTER NUMBER: S2100038261

Section 21 authorization letters are valid for a period of 6 months from the letter date, unless otherwise specified.

A progress report must be submitted once treatment is completed or on a reauthorization request

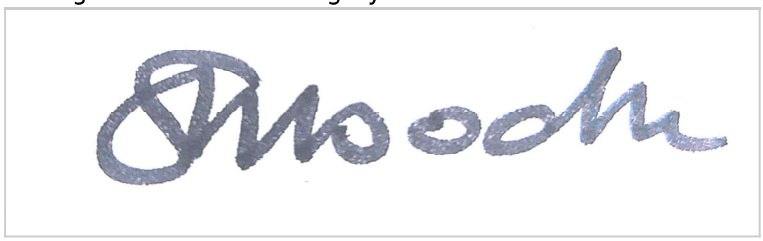
Comments:

No Data

Yours faithfully,

Shyamli Munbodh

Manager: Section 21 Category A Medicines



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REQUEST FOR QUOTATION FORM

- **Instruction to complete this Request for Quotation (RFQ)**
  PLEASE PROVIDE A QUOTE FOR THE FOLLOWING PRODUCT(S).
  PLEASE QUOTE ON THIS RFQ FORM AND ATTACH YOUR QUOTE WITH THE REQUESTED DETAILS.
  THE SECTIONS HIGHLIGHTED IN YELLOW MUST BE COMPLETED BY THE SUPPLIER.
- **THIS DOES NOT CONSTITUTE ANY OBLIGATION TO PROCURE THE ITEM AS THIS WILL BE SUBMITTED FOR CONSIDERATION TO PROVINCIAL PROCUREMENT UNITS TO SERVE AS A BUY OUT AGAINST CURRENT NON-COMPLIANT SUPPLIERS.**

ONLY RESPONSES FROM DULY REGISTERED SUPPLIERS WILL BE EVALUATED

REFERENCE NUMBER:	NORMAL		SECTION 21	X	S21RFQ188/2026
QUOTE ENQUIRY DATE	11/09/2026	QUOTE CLOSING DATE			18/09/2026
FOR CRITICAL DELIVERY, DELIVERY REQUESTED ON/BEFORE *(SCM Practitioner to Specify if applicable)*					

REQUESTING INSTITUTION CONTACT DETAILS

NAME OF REQUESTOR	Buhle Mbongo		
EMAIL ADDRESS	Buhle.Mbongo@health.gov.za		
PHONE No.	012 395 9539	FAX No.	N/A

PRODUCT INFORMATION

DESCRIPTION PER MPC	**Idarubicin 10mg INJ**		
TRADE DESCRIPTION	Idarub (Idarubicin) 10mg IV		
UNIT OF MEASURE	1's	PACK or BOX (*SIZE/ QUANTITY*)	1
QUANTITY REQUIRED	**350**		

TO BE COMPLETED BY THE SUPPLIER/ SERVICE PROVIDER

SUPPLIER CONTACT DETAILS (as per CSD)

DID YOU BID ITEM FOR TENDER	YES		NO	X	IF NO, WHY	**Section 21**
COMPANY NAME	Equity Pharmaceuticals (Pty) Ltd.					
SUPPLIER NUMBER	MAAA0007480					
SECURITY CODE						
SUPPLIER CODE (NDoH)						

CONTACT PERSON 1	NAME	**Ehrard van Zyl**		
	PHONE	**0123451747**	FAX	**012 345 1412**
	MOBILE	*072 040 8511*		
	E-MAIL	**ehrard@equitypharma.co.za**		
CONTACT PERSON 2	NAME	**Hannes Strydom**		
	PHONE	**012 345 1747**		

	MOBILE	*082 6161 954*
	E-MAIL	**hannes@equitypharma.co.za**

QUOTE DETAILS			
PRICE PER UNIT (INCL. VAT)	R 1015.45	TOTAL PRICE (INCL. DELIVERY & VAT)	R 355 407.50
VOLUMES AVAILABLE – 14DAYS	350 (7 days)		
VOLUMES AVAILABLE – 21DAYS			
VOLUMES AVAILABLE – 28DAYS			
VOLUMES AVAILABLE – 35DAYS			
VOLUMES AVAILABLE – 42DAYS			
VOLUMES AVAILABLE – 49DAYS			
VOLUMES AVAILABLE – 56DAYS			
VOLUMES AVAILABLE – 112DAYS			
QUOTE VALIDITY PERIOD	180 days		
NORMAL LEAD/DELIVERY TIME	3 days		

DEVIATION TO SPECIFICATION
COMMENTS:

DECLARATION BY SUPPLIER	
I hereby declare that in submitting this bid, there has been no consultation, communication, agreement or arrangement with any competitor/supplier regarding the price, quality, quantity, specifications and conditions or delivery particulars of the products or services to which this bid invitation relates.	
NAME	**Ehrard van Zyl**
CAPACITY	**Business Unit Manager: Specialist Medicine**
SIGNATURE *(OF A DULY AUTHORISED REPRESENTATIVE OF THE SUPPLIER)*	
DATE	**2026/09/18**

PROVINCIAL ESTIMATES	
Province	**Six Months Estimate**
DCS	**0**
EC-MT	**0**
EC-PE	**100**
FS	**0**
GP	**80**
KZN	**150**
LP	**0**

MP	0
NC	0
NW	0
SAMHS	0
WC	30
Please submit quotations to Section21Quotes@health.gov.za	

Please ensure that you include the following as part of the Quotation:

- Delivery Time (Weeks)
- Price (Vat Inclusive)
- Generic Name
- Trade Name
- Quotation on Official Company Letterhead
- Central Supplier Database Summary Report (CSD)
- Medicine Registration Certificate (Only for Locally Registered Products)
- *Artwork/Labelling
- *Package Insert/ Professional Information/Summary of Product Characteristics: (Please attach)
- *Manufacturer Certificate: (Please attach)
- *Country of Origin: (Please indicate)

*Additional items required when submitting a quote for a Section 21 Item (Unregistered Medicine)
All of the above is required to expedite the process in considering the quotation.

Please ***SUBMIT COMPLETED RFQ FORM AND QUOTATIONS ON AN OFFICIAL COMPANY LETTERHEAD***

NB:

- The supplier submitting the quotation must be the same entity which the provinces will place their orders
- The size of each individual attachment must not be more than 2MB (you may attach multiple files in one email but collectively they should not be more than 2MB in size).
- Please ensure that you provide all prescribed documentation that is outlined on page two of this RFQ.
- The confirmation letter from manufacturer to Supply South Africa with Bivalent oral Poliomyelitis Vaccine (bOPV) must be provided (only in cases of Bivalent oral Poliomyelitis Vaccine RFQ)
- Kindly be advised that a picture format of an Artwork shall not be accepted. Artwork must be in pdf or word format only.
- All prices must please be submitted in two decimals and in ZAR.
- If submitting more than one quotation, please make sure that your subject line includes e.g., 1 of 2 or 1 of 3 etc.
- Any submission with missing documentation shall not be considered.
- Any submission with blurry relevant documents shall not be considered.
- The only electronic GMP Certificate considered is that from EUDRA
- CSD must be updated for the current month of the RFQ date.
- **Email subject line for responses with quotes must be kept unchanged from the originally sent RFQ email.**

Please ***SUBMIT COMPLETED RFQ FORM AND QUOTATIONS ON AN OFFICIAL COMPANY LETTERHEAD***

EQUITY
PHARMACEUTICALS

18/09/2026

Equity Pharmaceuticals (Pty) Ltd.
1997/009942/07

+27 12 345 1747
+27 12 345 1412
equity@equitypharma.co.za

www.clinigengroup.com
www.equitypharma.co.za

National Department of Health

Directorate: Affordable Medicines

E-mail: Buhle.Mbongo@health.gov.za

Attention: Ms Buhle Mbongo

Dear B Mbongo

Re: Request for quotation – Idarubicin 10mg INJ – Section 21 Supply

Trust you are well. Please find below our quotation for Idarub (Idarubicin) 10mg injections supplied under section 21 terms.

• Quantity:	**350 packs**
• Delivery Time (Weeks):	**7 days**
• Price (Vat Inclusive):	**R 1015.45 incl. vat per vial**
• Generic Name:	**Idarubicin 10mg INJ**
• Trade Name:	**Idarub (Idarubicin) 10mg injection**
• Packaging:	**1 x vial**
• Specifications:	**Each vial containing 10mg Idarubicin**
• Shelf Life:	**36 months**
• Package Insert:	**Please find attached**
• Manufacturer:	**Kocak Farma Ilac Ve Kimya Sanayi A.S.**
• Country of Origin:	**Turkey**

Please note that the immediate availability of the product is conditioned on the manufacturer receiving notice of our order as soon as possible. Unfortunately, the stock cannot be reserved for our purposes for too long.

We look forward to your response.

Please contact me if you require any additional information.

Kind Regards

Ehrard van Zyl

18/09/2026

Equity Pharmaceuticals (Pty) Ltd.
1997/009942/07

+27 12 345 1747
+27 12 345 1412
equity@equitypharma.co.za

www.clinigengroup.com
www.equitypharma.co.za

QUOTATION # 20260918

TO: National Department of Health

TEL : 066 261 4234
FAX :
Email : Buhle.Mbongo@health.gov.za

CONTACT PERSON / PATIENT : Buhle Mbongo

NB IMPORTED AND SUPPLIED UNDER SECTION 21 TERMS

PRODUCT CODE	DESCRIPTION	PACK SIZE	QUANTITY	PRICE EXCL	TOTAL INCL
	Idarub (Idarubicin) 10mg IV	1 vial	1	R 883.00	R 1015.45
			350	**R 309 050.00**	**R 355 407.50**
			350	**R 309 050.00**	**R 355 407.50**

Valid for 180 days

Signature: _____

Date: 18/09/2026

Approved by: Ehrard van Zyl

SUMMARY OF PRODUCT CHARACTERISTICS

MEDICAL / PHARMACEUTICAL REGULATORY DOCUMENTATION

STERILE CYTOTOXIC

1. NAME OF THE MEDICINAL PRODUCT

IDARUB 10 mg IV lyophilized powder for solution in vial

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Idarubicin Hydrochloride — 10 mg per vial.

Excipients with known effect:

Lactose monohydrate (bovine origin) — 100 mg. For the full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Lyophilized powder.

Orange-red lyophilized powder supplied in a transparent glass vial.

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Idarubicin is an antimitotic and cytotoxic agent, mainly used in combination chemotherapy regimens with other cytotoxic agents. Idarubicin is indicated for the treatment of the following malignancies:

- **Acute Myeloid Leukemia (AML) / Acute Non-Lymphocytic Leukemia (ANLL):** Includes all French-American-British (FAB) classification subtypes from M1 to M7. Indicated in adults for first-line remission induction therapy or for remission induction in relapsed or refractory cases.
- **Acute Lymphocytic Leukemia (ALL):** Indicated as second-line treatment in adults and pediatric populations.

4.2. Posology and Method of Administration

Posology: When administering IDARUB, the patient's hematological status must be monitored; when used in combination with other cytotoxic agents, the dosages of those agents must be taken into account.

Frequency and Duration of Administration:

Acute Myeloid Leukemia (AML / ANLL):

- The recommended dose in combination with cytarabine is $12\ mg/m^2$ daily IV for 3 consecutive days.
- An alternative recommended schedule for single-agent or combination use in AML/ANLL is $8\ mg/m^2$ daily IV for 5 consecutive days.

Acute Lymphocytic Leukemia (ALL):

- **Adults:** As single-agent therapy, the recommended dose in ALL is $12\ mg/m^2$ daily IV for 3 consecutive days.
- Administration of the second course should be delayed in cases of severe mucositis until toxicity resolves, and a 25% dose reduction is recommended.

Method of Administration: For intravenous (IV) use only.

To prepare the solution, dissolve the contents of the 10 mg vial in 10 mL of Water for Injections. Once proper intravenous needle placement is ensured, the reconstituted solution should be administered via a freely flowing intravenous infusion line over a period of 5 to 10 minutes. This method minimizes the risk of perivenous extravasation or thrombosis, which could lead to severe cellulitis and necrosis. Repeated injections into the same vein or injections into small veins may lead to venous sclerosis. Dosing is generally calculated based on Body Surface Area (BSA).

4.2. Posology and Method of Administration (Continued)

Additional Information on Special Populations:

- **Hepatic/Renal Impairment:** Due to limited data in patients with hepatic and/or renal impairment, specific dose recommendations cannot be made. Dose reduction should be considered in patients with serum bilirubin and/or creatinine levels exceeding 2.0 mg/dL (see Section 4.4). IDARUB must not be administered to patients with severe hepatic and/or renal impairment (see Section 4.3).
- **Pediatric Population:** When used as a single agent in ALL, the recommended dose is $10\ mg/m^2$ daily IV for 3 consecutive days.
- **Geriatric Population:** In patients over 60 years of age, congestive heart failure, severe arrhythmias, chest pain, myocardial infarction, and asymptomatic drops in left ventricular ejection fraction (LVEF) occurred more frequently during induction therapy compared to younger patients (see Section 4.8).

4.3. Contraindications

- Known hypersensitivity to idarubicin hydrochloride, any of the excipients, or to other anthracyclines or anthracenediones.
- Severe hepatic impairment.
- Severe renal impairment.
- Untreated infections.
- Severe myocardial insufficiency.
- Recent myocardial infarction.
- Severe cardiac arrhythmias.
- Persistent myelosuppression.
- Prior treatment with maximum cumulative doses of idarubicin and/or other anthracyclines or anthracenediones (see Section 4.4).
- Breastfeeding must be discontinued during treatment (see Section 4.6).

4.4. Special Warnings and Precautions for Use

BLACK BOX WARNINGS & CRITICAL PRECAUTIONS

1. IDARUB must be administered strictly via a freely flowing intravenous infusion. Never administer intramuscularly or subcutaneously. Do NOT administer intrathecally. Extravasation during administration may cause severe local tissue necrosis.
2. When used with other anthracyclines, IDARUB may cause myocardial toxicity leading to congestive heart failure. Cardiotoxicity is more common in patients with prior anthracycline exposure or pre-existing cardiac disease.
3. As with antileukemic agents in general, severe myelosuppression occurs when IDARUB is used at effective therapeutic doses.
4. IDARUB should be administered under the supervision of a physician experienced in leukemia chemotherapy in centers equipped with adequate laboratory and supportive facilities to monitor tolerance and manage toxicity risks.
5. Dose reductions may be required in patients with impaired liver or kidney function (see Section 4.2).

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

Hematologic Toxicity: Idarubicin is a potent bone marrow suppressant. Severe myelosuppression occurs in all patients at therapeutic doses. Full hematological profiles, including differential white blood cell counts, must be evaluated before and during each treatment cycle. Reversible leukopenia/granulocytopenia (neutropenia) is the predominant acute dose-limiting toxicity. Neutrophil and platelet counts reach their nadir 10 to 14 days post-administration, usually recovering by week 3. Severe myelosuppression may lead to fever, infection, sepsis, septic

4.4. Special Warnings and Precautions for Use (Continued)

Secondary Leukemia: Secondary leukemia (with or without a pre-leukemic phase) has been reported in patients treated with anthracyclines including idarubicin. This is more common when combined with DNA-damaging antineoplastic agents, when heavily pretreated, or when anthracycline doses are escalated. These leukemias may have a 1- to 3-year latency period.

Cardiac Function: Cardiotoxicity is a known risk of anthracycline therapy and can present as early (acute) or late (delayed) events.

- *Early (Acute) Events:* Consist mainly of sinus tachycardia and/or non-specific ST-T wave ECG changes. Tachyarrhythmias (including premature ventricular contractions and ventricular tachycardia), bradycardia, and AV or bundle branch blocks have been reported. These early effects are generally not predictive of subsequent delayed cardiotoxicity and rarely require treatment discontinuation.
- *Late (Delayed) Events:* Usually develop late during therapy or within 2–3 months post-treatment, though manifestations months to years later have been reported. Delayed cardiomyopathy presents as a decrease in LVEF and/or signs/symptoms of congestive heart failure (CHF) such as dyspnea, pulmonary edema, peripheral edema, cardiomegaly, hepatomegaly, oliguria, ascites, pleural effusion, and gallop rhythm. Subacute effects like pericarditis/myocarditis are also reported. Life-threatening CHF is the most severe form of anthracycline-induced cardiomyopathy and represents the cumulative dose-limiting toxicity of the drug.

While a cumulative dose limit for IDARUB has not been fully established, idarubicin-related cardiomyopathy was reported in 5% of patients receiving cumulative IV doses of $150–290\ mg/m^2$. Cardiac function should be evaluated before initiating treatment. Quantitative baseline and periodic assessment of LVEF using MUGA scan or Echocardiography (ECHO) is recommended, especially in patients with risk factors (active or occult cardiovascular disease, prior radiotherapy to mediastinal area, prior anthracycline treatment, or concomitant use of cardiotoxic drugs like trastuzumab). Trastuzumab has an elimination half-life of ~28.5 days and can persist for up to 24 weeks; anthracycline therapy should be avoided for up to 24 weeks after stopping trastuzumab when possible.

Gastrointestinal: Idarubicin is emetogenic. Mucositis (mainly stomatitis, less frequently esophagitis) appears early after administration and may progress to mucosal ulcerations. In patients with active GI disease at risk of hemorrhage or perforation, the benefit of treatment must be weighed against potential risks.

Tumor Lysis Syndrome (TLS): Idarubicin may induce hyperuricemia as a consequence of extensive purine catabolism accompanying drug-induced rapid lysis of neoplastic cells. Blood uric acid, potassium, calcium, phosphate, and creatinine levels should be evaluated. Hydration, urine alkalinization, and allopurinol prophylaxis can minimize TLS complications.

Excipient Warning: Patients with rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption should not take this medicine.

4.5. Interactions with Other Medicinal Products and Other Forms of Interaction

- **Other Myelosuppressive Agents:** Combined chemotherapy with other drugs causing bone marrow suppression may produce additive myelosuppressive effects.
- **Cardioactive Compounds:** Concomitant use with drugs such as calcium channel blockers requires monitoring of cardiac function throughout treatment.
- **Radiotherapy:** Radiation therapy administered concurrently or within 2–3 weeks prior to IDARUB treatment may result in increased myelosuppression.
- **Incompatibilities:** Alkaline solutions cause long-term drug degradation. IDARUB must not be mixed with heparin as precipitation may occur. Mixing with other drugs is not recommended.

4.6. Fertility, Pregnancy and Lactation

Pregnancy (Category D): Idarubicin has harmful pharmacological effects on pregnancy, the fetus, and the newborn. In vitro and in vivo studies demonstrate embryotoxicity and teratogenicity. IDARUB should not be used during pregnancy unless the potential benefit outweighs the potential risk to the fetus. If used, the patient must be informed of the potential hazards.

Lactation: It is unknown whether idarubicin or its metabolites are excreted in human milk. Mothers must be advised not to breastfeed while receiving IDARUB chemotherapy. IDARUB is contraindicated during lactation (see Section 4.3).

Fertility: Idarubicin can induce chromosomal damage in human sperm cells. Men undergoing treatment must use effective contraceptive measures during therapy and seek advice on sperm preservation prior to treatment due to possible irreversible infertility.

4.7. Effects on Ability to Drive and Use Machines

The effect of IDARUB on the ability to drive and use machines has not been systematically evaluated. Caution should be exercised when driving or operating machinery.

4.8. Undesirable Effects

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

System Organ Class	Frequency	Adverse Reactions
Infections and Infestations	Very common Uncommon	Infections Sepsis, septicemia
Neoplasms (Benign, Malignant)	Uncommon	Secondary leukemia (AML, Myelodysplastic syndrome)
Blood & Lymphatic System	Very common	Anemia, severe leukopenia, neutropenia, thrombocytopenia
Immune System Disorders	Very rare	Anaphylaxis
Endocrine / Metabolism	Very common Uncommon	Anorexia Hyperuricemia
Nervous System Disorders	Rare	Cerebral hemorrhage
Cardiac Disorders	Common Uncommon Very rare	Bradycardia, sinus tachycardia, tachyarrhythmias, asymptomatic LVEF reduction, congestive heart failure (CHF) ECG abnormalities (non-specific ST changes), myocardial infarction Pericarditis, myocarditis, AV & bundle branch blocks
Vascular Disorders	Common Uncommon Very rare	Local phlebitis, thrombophlebitis Shock Thromboembolism, flushing
Gastrointestinal Disorders	Very common Common Uncommon Very rare	Nausea, vomiting, mucositis/stomatitis, diarrhea, abdominal pain/burning sensation Gastrointestinal hemorrhage, abdominal pain Esophagitis, colitis (severe enterocolitis/neutropenic enterocolitis) Gastric erosions or ulceration
Hepatobiliary Disorders	Common	Elevations in bilirubin and liver enzymes
Skin & Subcutaneous Tissue	Very common Common Uncommon	Alopecia Rash, pruritus, hypersensitivity of irradiated skin Skin and nail hyperpigmentation, urticaria

4.9. Overdose

Very high doses of IDARUB are expected to cause acute myocardial toxicity within 24 hours and severe myelosuppression within 1 to 2 weeks. Gastrointestinal hemorrhage and severe mucosal damage may occur. Supportive care, including platelet transfusions, antibiotics, and symptomatic treatment for mucositis, is required. Delayed cardiac failure has been observed up to several months following anthracycline overdose. IDARUB is not removed by peritoneal dialysis or hemodialysis due to extensive tissue binding and high distribution volume. No specific antidote exists.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

Pharmacotherapeutic Group: Anthracyclines and related substances **| ATC Code:** L01DB06

Mechanism of Action: Idarubicin is a DNA-intercalating anthracycline that interacts with Topoisomerase II and inhibits nucleic acid synthesis. Modification at position 4 of the anthracycline structure imparts high lipophilicity, leading to higher cellular uptake compared to doxorubicin or daunorubicin.

Efficacy and Safety: In vitro studies demonstrate lower cross-resistance to idarubicin in anthracycline-resistant cell lines compared to doxorubicin and daunorubicin. Animal cardiotoxicity studies show a higher therapeutic index for idarubicin than daunorubicin or doxorubicin. Its primary active metabolite, idarubicinol, displays antitumoral activity both in vitro and in vivo, with significantly lower cardiotoxicity than the parent compound in animal models. Plasma protein binding is at least 95%.

5.2. Pharmacokinetic Properties

Absorption & Distribution: Peak cellular concentrations in nucleated blood and bone marrow cells are achieved minutes after injection. Concentrations of idarubicin and idarubicinol in nucleated blood and marrow cells are over 100-fold higher than plasma levels. Plasma protein binding is 97% for idarubicin and 94% for idarubicinol. Distribution volume is very high, reflecting extensive tissue binding.

Biotransformation: The primary active metabolite is idarubicinol, which contributes to the overall cytotoxic efficacy.

Elimination: In patients with normal organ function, terminal plasma elimination half-life ($T_{1/2}$) is 11–25 hours for idarubicin and 41–69 hours for idarubicinol. Excretion occurs mainly via bile and urine as idarubicinol. Cellular half-life of idarubicinol is approximately 72 hours.

Special Populations: In pediatric leukemia patients receiving $4.2–13.3\ mg/m^2$ daily for 3 days, drug clearance was dose-independent. Idarubicinol was detected in 20 out of 21 CSF samples (mean $0.51\ ng/mL$) 18–30 hours post-dose. Hepatic/renal impairment reduces clearance, resulting in higher systemic exposure.

5.3. Preclinical Safety Data

Idarubicin is mutagenic and carcinogenic in rats. Reproduction studies demonstrate embryotoxicity and teratogenicity in rats at $1.2\ mg/m^2/day$ (1/10th human dose) and embryotoxicity in rabbits at $2.4\ mg/m^2/day$. In male dogs, administration of $1.8\ mg/m^2$ 3 times weekly for 13 weeks produced testicular atrophy and inhibition of spermatogenesis, which were not fully reversible after an 8-week recovery period.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Lactose monohydrate (bovine origin).

6.2. Incompatibilities

IDARUB must not be mixed with other medicinal products unless compatibility is established. Precipitation occurs with heparin. Prolonged contact with alkaline solutions causes drug degradation.

6.3. Shelf Life

24 months.

6.4. Special Precautions for Storage

Store lyophilized powder vial below 25°C at room temperature.

Reconstituted Solution: Chemically stable for up to 48 hours at 2–8°C and 24 hours at room temperature (20–25°C). For good pharmaceutical practice, it is recommended that reconstituted solutions not be stored for more than 24 hours at 2–8°C. Contains no antibacterial preservatives; use immediately upon reconstitution.

6.5. Nature and Contents of Container

Clear Type I glass vial sealed with a lyophilization stopper and flip-off aluminum cap.

6.6. Special Precautions for Disposal and Handling

Reconstitute the 10 mg vial with 10 mL Water for Injections. Due to cytotoxic nature, observe strict handling precautions:

- Personnel must be trained in reconstitution and administration; pregnant personnel must avoid contact.
- Wear protective clothing: disposable gloves, safety goggles, gowns, and masks. Reconstitute in a dedicated safety hood (laminar flow).
- Spills: Treat with dilute sodium hypochlorite (1% available chlorine) followed by water.
- Accidental contact: Rinse skin immediately with water/soap or sodium bicarbonate solution; flush eyes with water for 15 minutes.

7. MARKETING AUTHORIZATION HOLDER

Koçak Farma İlaç ve Kimya Sanayi A.Ş.
Mahmutbey Mah. 2477. Sok. No: 23, Bağcılar / İstanbul, Türkiye
Tel: +90 (212) 410 39 50 | Fax: +90 (212) 447 61 65

8. MA NUMBER

2016/167

9. AUTHORIZATION DATE

First Registration: 01.03.2016
Renewal Date: —

10. REVISION DATE

—


Steril- Apirojen
1Flakon
İDARUB 10 mg
IV Liyofilize Toz İçeren Flakon
İdarubisin hidroklorür
Sitotoksik ajan
KOÇAK FARMA