DOXORUBICIN HYDROCHLORIDE, LIPOSOMAL- doxorubicin hydrochloride injection, suspension, liposomal
Baxter Healthcare Corporation

Disclaimer: This drug has not been found by FDA to be safe and effective, and this labeling has not been approved by FDA. For further information about unapproved drugs, click here.

Doxorubicin Hydrochloride Liposome Injection

HEALTH CARE PROVIDER LETTER

Baxter

Important Prescribing Information

November 17, 2023

Subject: Temporary importation of CAELYX (DOXOrubicin hydrochloride liposome injection) with foreign, non-U.S. labeling to address drug shortages

Dear Healthcare Professional,

Due to a potential critical shortage of DOXIL (DOXOrubicin Hydrochloride liposome injection) products in the United States (U.S.) market, Baxter Healthcare Corporation (Baxter) is coordinating with the U.S. Food and Drug Administration (FDA) to temporarily import CAELYX pegylated liposomal (DOXOrubicin hydrochloride liposome injection) into the U.S. market. CAELYX is marketed in the United Kingdom (U.K.) and is not FDA-approved in the U.S.

At this time, no other entity except Baxter is authorized by the FDA to import or distribute this product in the United States.

Effective immediately, and during this temporary period, Baxter will offer the following:

Product name and description	Presentation	Packaging	GTIN	Lot/Expiration	NDC
CAELYX pegylated liposomal 2 mg/ml concentrate for solution for infusion (DOXOrubicin hydrochloride liposome injection)	10 mL glass vial	1 vial per carton	25413765812280	NCZSG00 31/10/24	Vial: 0338-9581-01 Carton: 0338-9581-02

It is important to note the following:

- The carton labeling and container label of Caelyx does not include the warning, "Liposomal formulation – do not substitute for doxorubicin hydrochloride"
- Caelyx will be available only by prescription in the U.S. However, the imported product does not have the statement "Rx only" on the labeling.
- The barcode on the imported product label may not register accurately on the U.S. scanning systems. The imported products do not have a linear barcode on the vial. Institutions should manually input the product into their systems to confirm that barcode systems do not provide incorrect information when the product is scanned. Alternative procedures should be followed to assure that the correct drug product is being used and administered to individual patients.

There are some key differences in the labeling between the FDA-approved DOXIL and the imported product. Please refer to the product comparison table at the end of this letter.

Please refer to the FDA-approved package insert for DOXIL's full prescribing information at DailyMed (click HERE).

Reporting Adverse Events:

To report product quality issues, please contact Baxter Product Surveillance at 1-800-437-5176.

To report adverse events associated with these imported products, please call Baxter at 1-866-888-2472, or fax: 1-800-759-1801. Adverse events, medication errors, or quality problems experienced with the use of this product may also be reported to the FDA's MedWatch Adverse Event Reporting program either online, by regular mail or by fax:

- Complete and submit the report Online: www.fda.gov/medwatch/report.htm
- Regular mail or Fax: Download form http://www.fda.gov/MedWatch/getforms.htm or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178 (1-800-332-0178).

To place an order, please contact Baxter's Center for Service by calling 1-888-229-0001.

If you have any questions about the information contained in this letter or the use of the imported product, please contact Baxter's Medical Information Service at 1-800-933-0303.

Sincerely,

Arvind Tekumal

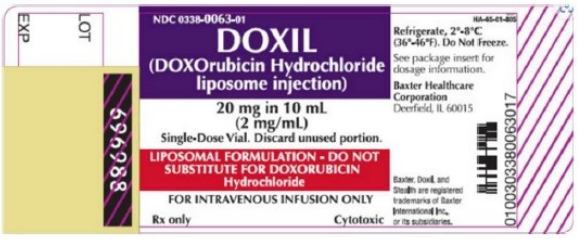
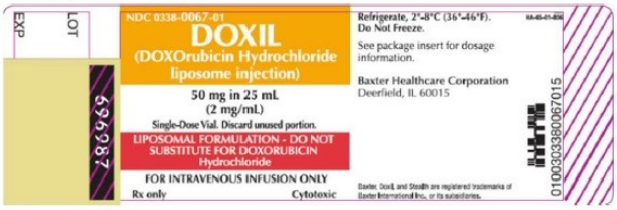
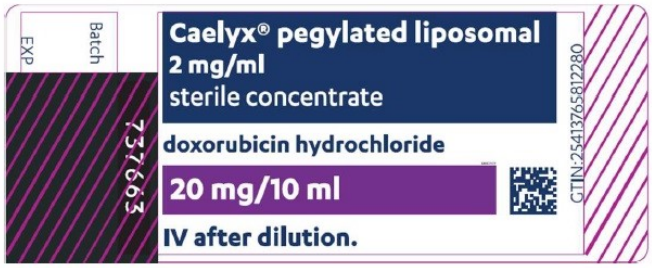
Arvind Tekumal
Sr. Director US Hospital Pharmaceutical Generic Injectable Marketing
Baxter Healthcare Corporation

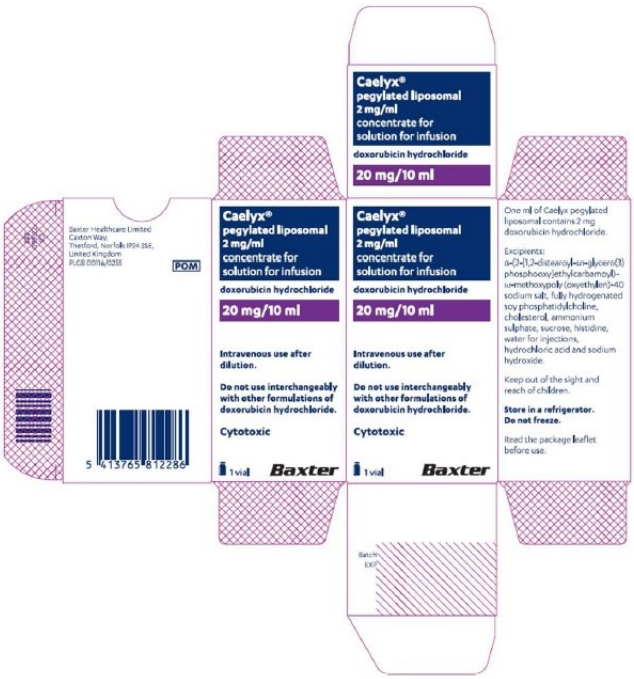
	FDA-APPROVED PRODUCT	IMPORTED PRODUCT	Action to Take
	DOXIL (DOXOrubcin Hydrochloride liposome injection)	CAELYX pegylated liposomal 2 mg/ml concentrate for solution for infusion (UK) (DOXOrubicin hydrochloride liposome injection)	
Prescribing Information	Packaged with complete prescribing information	Packaged with local prescribing information	Please refer to package insert for full prescribing information (click HERE for USPI). Full UK SPC available HERE.
How Supplied and Composition	20 mg/10 mL (2 mg/mL) vial 50 mg/25 mL (2 mg/mL) vial Each mL contains: doxorubicin hydrochloride – 2 mg cholesterol – 3.19 mg Fully hydrogenated soy phosphatidylcholine (HSPC) – 9.58 mg N-(carbonyl-methoxypolyethylene glycol 2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine sodium salt (MPEG-DSPE) –3.19 mg Ammonium sulfate – approximately 0.6 mg Histidine – 1.55 mg Hydrochloric acid and/or sodium hydroxide for pH adjustment Sucrose – 94 mg Water for injection – q.s. pH range – 6.0 to 7.0	20 mg/10 mL (2 mg/mL) vial Each mL contains: doxorubicin hydrochloride – 2 mg cholesterol – 3.19 mg Fully hydrogenated soy phosphatidylcholine (HSPC) – 9.58 mg N-(carbonyl-methoxypolyethylene glycol 2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine sodium salt (MPEG-DSPE) –3.19 mg Ammonium sulfate – approximately 0.6 mg Histidine – 1.55 mg Hydrochloric acid and/or sodium hydroxide for pH adjustment Sucrose – 94 mg Water for injection – q.s. pH range – 6.0 to 7.0	No differences in formulation exist between DOXIL and CAELYX

	FDA-APPROVED PRODUCT	IMPORTED PRODUCT	Action to Take
	DOXIL (DOXOrubcin Hydrochloride liposome injection)	CAELYX pegylated liposomal 2 mg/ml concentrate for solution for infusion (UK) (DOXOrubicin hydrochloride liposome injection)	
Indications	• Ovarian Cancer in patients with ovarian cancer whose disease has progressed or recurred after platinum-based chemotherapy • AIDS-Related Kaposi's Sarcoma in patients after failure of prior systemic chemotherapy or intolerance to such therapy • Multiple Myeloma in combination with bortezomib in patients who have not previously received bortezomib and have received at least one prior therapy	• Metastatic breast cancer as monotherapy for patients with where there is an increased cardiac risk • Advanced ovarian cancer in women who have failed a first-line platinum-based chemotherapy regimen • Progressive multiple myeloma in combination with bortezomib in patients who have received at least one prior therapy and who have already undergone or are unsuitable for bone marrow transplant • AIDS-related Kaposi's sarcoma (KS) in patients with low CD4 counts (< 200 CD4 Lymphocytes/mm3) and extensive mucocutaneous or visceral disease.	DOXIL has not been approved for use in metastatic breast cancer by the U.S. FDA. Complete indications and dosages are available in full prescribing information.
Boxed Warning	WARNING: CARDIOMYOPATHY AND INFUSION-RELATED REACTIONS • DOXIL liposomal infusion can cause myocardial damage, including acute left ventricular failure. The risk of cardiomyopathy was 11% when the cumulative anthracycline dose was between 450 mg/m^2 to 550 mg/m^2. Assess left ventricular cardiac function prior to initiation of DOXIL liposomal infusion and during and after treatment. • Serious, life-threatening, and fatal infusion-related reactions can occur with DOXIL liposomal infusion Acute infusion-related reactions occurred in 11% of patients with solid tumors. Withhold DOXIL liposomal infusion for infusion-related reactions and resume at a reduced rate. Discontinue DOXIL liposomal infusion for serious or life-threatening infusion-related reactions.	No Boxed Warning. Similar warnings are listed in Section 4.4 (Special Warnings and Precautions for Use) of the CAELYX SmPC.	Please refer to package insert for full prescribing information (click HERE). Full UK SPC available HERE.

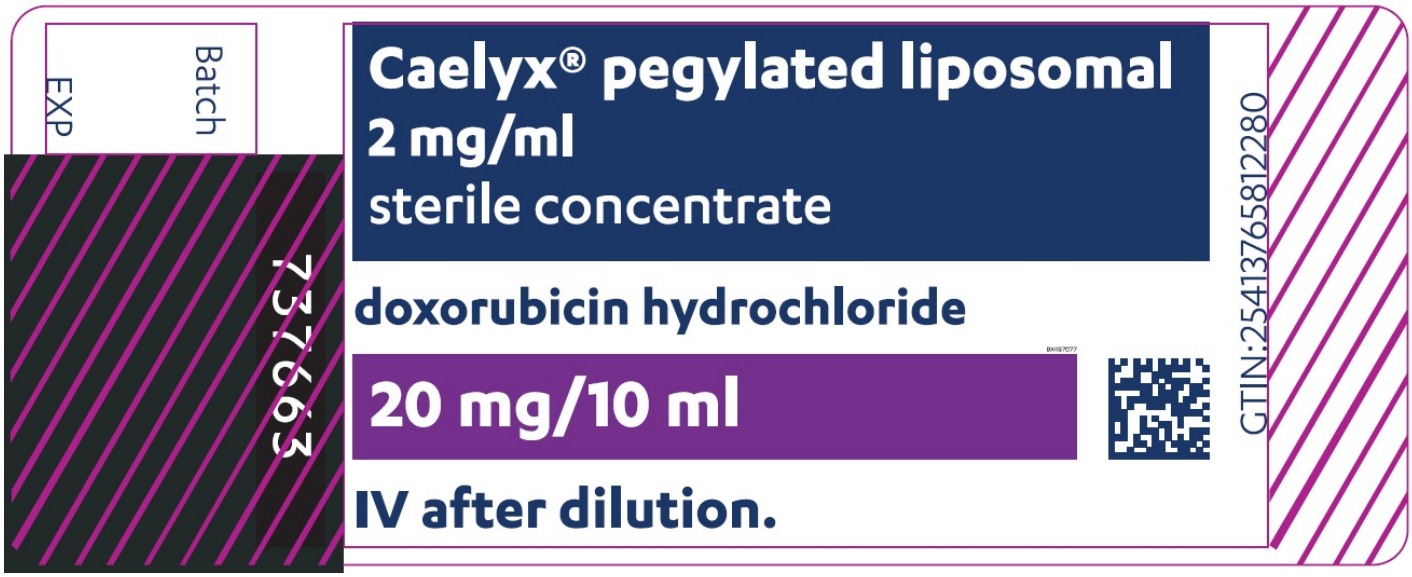
	FDA-APPROVED PRODUCT	IMPORTED PRODUCT	Action to Take
	DOXIL (DOXOrubcin Hydrochloride liposome injection)	CAELYX pegylated liposomal 2 mg/ml concentrate for solution for infusion (UK) (DOXOrubicin hydrochloride liposome injection)	
Administration and Use	Intravenously by infusion as directed in prescribing information	Intravenously by infusion as specified in complete prescribing information	Complete instructions are available in full prescribing information.
	Do not substitute DOXIL liposomal infusion for other doxorubicin hydrochloride products	CAELYX pegylated liposomal exhibits unique pharmacokinetic properties and must not be used interchangeably with other formulations of doxorubicin hydrochloride	
	Dilution Prior to Administration Do not administer as an undiluted suspension or as an intravenous bolus.	Dilution Prior to Administration Do not administer CAELYX pegylated liposomal as a bolus injection or undiluted dispersion.	
Handling Procedures	Handling Procedures - General Inspect parenteral drug products visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if a precipitate or foreign matter is present. Do not use with in-line filters. DOXIL liposomal infusion is a cytotoxic drug. Follow applicable special handling and disposal procedures. If DOXIL liposomal infusion comes into contact with skin or mucosa, immediately wash thoroughly with soap and water.	Do not use material that shows evidence of precipitation or any other particulate matter. Caution must be exercised in handling CAELYX pegylated liposomal dispersion. The use of gloves is required. If CAELYX pegylated liposomal comes into contact with skin or mucosa, wash immediately and thoroughly with soap and water. CAELYX pegylated liposomal must be handled and disposed of in a manner consistent with that of other anticancer medicinal products in accordance with local requirements. Aseptic technique must be strictly observed since no preservative or bacteriostatic agent is present in CAELYX pegylated liposomal. Do not use with in-line filters.	Complete instructions are available in full prescribing information.

	FDA-APPROVED PRODUCT	IMPORTED PRODUCT	Action to Take
	DOXIL (DOXOrubcin Hydrochloride liposome injection)	CAELYX pegylated liposomal 2 mg/ml concentrate for solution for infusion (UK) (DOXOrubicin hydrochloride liposome injection)	
Compatibility and Stability	Dilute DOXIL liposomal infusion doses up to 90 mg in 250 mL of 5% Dextrose Injection, USP prior to administration. Dilute doses exceeding 90 mg in 500 mL of 5% Dextrose Injection, USP prior to administration. Refrigerate diluted DOXIL liposomal infusion at 2°C to 8°C (36°F to 46°F) and administer within 24 hours.	The appropriate dose of CAELYX pegylated liposomal must be diluted in 5% (50 mg/ml) glucose solution (5% Dextrose Injection, USP) for infusion prior to administration. For doses < 90 mg, dilute CAELYX pegylated liposomal in 250 ml, and for doses ≥ 90 mg, dilute CAELYX pegylated liposomal in 500 ml. The use of any diluent other than 5% (50 mg/ml) glucose solution for infusion, or the presence of any bacteriostatic agent such as benzyl alcohol may cause precipitation of CAELYX pegylated liposomal. Chemical and physical in-use stability of diluted CAELYX has been demonstrated for 24 hours at 2°C to 8°C. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and should not be longer than 24 hours at 2°C to 8°C.	Complete instructions are available in full prescribing information.
Storage Conditions	Refrigerate unopened vials of DOXIL (doxorubicin hydrochloride liposome injection) at 2°C- 8°C (36°F- 46°F). Do not freeze. Discard unused portion.	Store in a refrigerator (2°C – 8°C). Do not freeze. Partially used vials must be discarded.	Complete instructions are available in full prescribing information.

FDA-APPROVED PRODUCTS	IMPORTED PRODUCT
DOXIL (DOXOrubcin Hydrochloride liposome injection) 20 mg/10 mL Vial (USA) 50 mg/25 mL Vial (USA)	CAELYX pegylated liposomal 2 mg/ml concentrate for solution for infusion 20 mg/10 mL Vial (UK) (DOXOrubicin hydrochloride liposome injection)
CONTAINER LABELS	
20 mg/10 mL vial  50 MG/25 mL vial  	20 mg/10 mL vial 

FDA-APPROVED PRODUCTS	IMPORTED PRODUCT
DOXIL (DOXOrubcin Hydrochloride liposome injection) 20 mg/10 mL Vial (USA) 50 mg/25 mL Vial (USA)	CAELYX pegylated liposomal 2 mg/ml concentrate for solution for infusion 20 mg/10 mL Vial (UK) (DOXOrubicin hydrochloride liposome injection)
CONTAINER CARTONS	
20 mg/10 mL vial  50 mg/25 mL vial 	20 mg/10 mL vial 

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL – 20 mg/10 mL

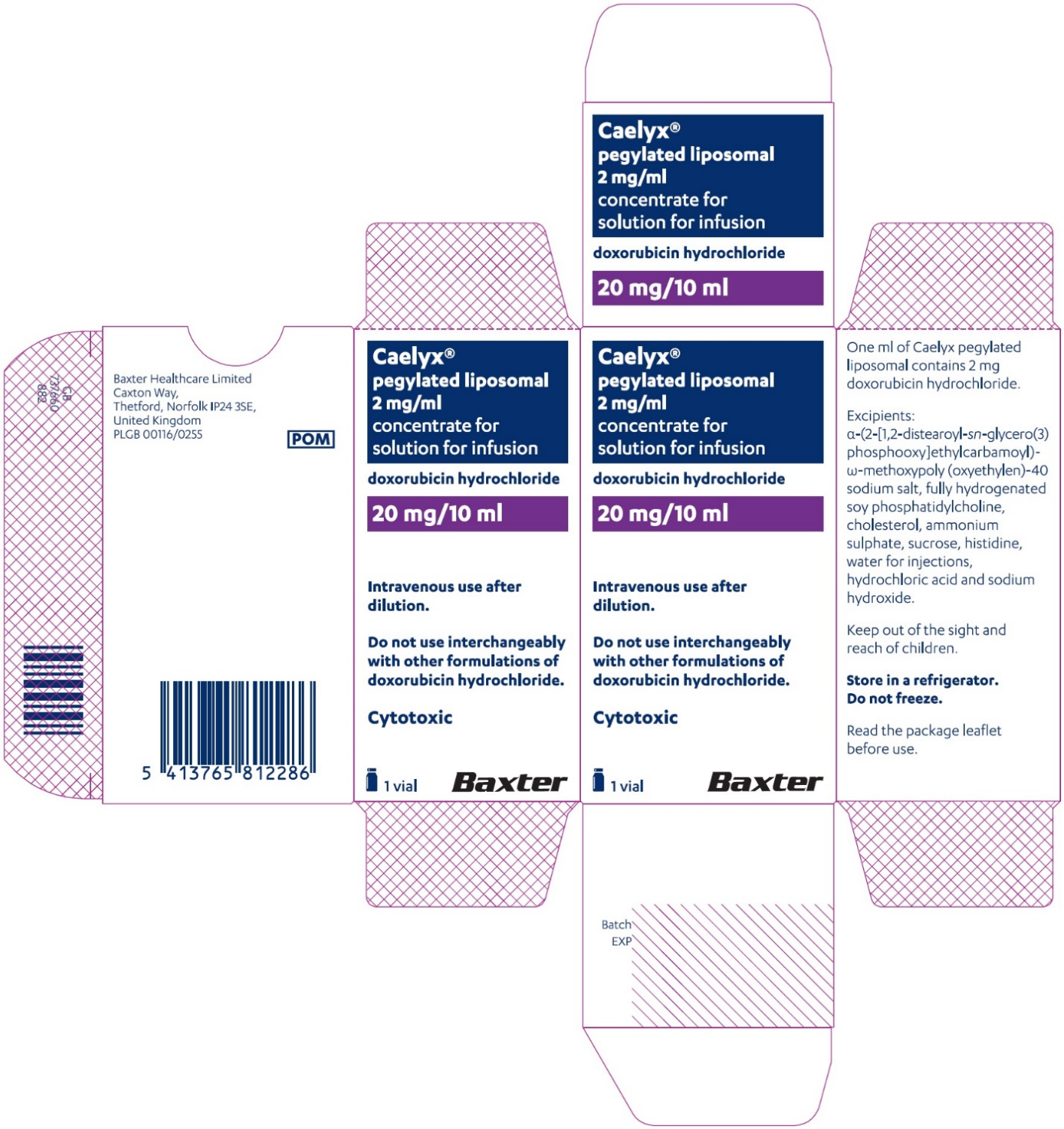


Caelyx® pegylated liposomal
2 mg/ml
sterile concentrate

doxorubicin hydrochloride

20 mg/10 mL

IV after dilution.



Caelyx®
pegylated liposomal
2 mg/ml
concentrate for
solution for infusion
doxorubicin hydrochloride

20 mg/10 mL

Intravenous use after

dilution.

Do not use interchangeably with other formulations of doxorubicin hydrochloride.

Cytotoxic

1 vial

***Baxter* Logo**

One ml of Caelyx pegylated liposomal contains 2 mg doxorubicin hydrochloride.

Excipients: α-(2-[1,2-distearoyl-*sn*-glycero(3) phosphooxy]ethylcarbamoyl) -ϖ-methoxypoly(oxyethylen)-40 sodium salt, fully hydrogenated soy phosphatidylcholine, cholesterol, ammonium sulphate, sucrose, histidine, water for injections, hydrochloric acid and sodium hydroxide.

Keep out of the sight and reach of children.

Store in a refrigerator.
Do not freeze.

Read the package leaflet before use.

Baxter Healthcare Limited

Caxton Way,

Thetford,

Norfolk,

IP24 3SE,

United Kingdom

PLGB 00116/0255

DOXORUBICIN HYDROCHLORIDE, LIPOSOMAL

doxorubicin hydrochloride injection, suspension, liposomal

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0338-9581
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
doxorubicin hydrochloride (UNII: 82F2G7BL4E) (doxorubicin - UNII:80168379AG)	doxorubicin hydrochloride	2 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM N-(CARBONYL-METHOXYPOLYETHYLENE GLYCOL 2000)-1,2-DISTEAROYL-SN-GLYCERO-3-PHOSPHOETHANOLAMINE (UNII: 3L6NN8ZZKU)	3.19 mg in 1 mL
hydrogenated soybean lecithin (UNII: H1109Z9J4N)	9.58 mg in 1 mL
cholesterol (UNII: 97C5T2UQ7J)	3.19 mg in 1 mL
ammonium sulfate (UNII: SU46BAM238)	0.6 mg in 1 mL
histidine (UNII: 4QD397987E)	1.55 mg in 1 mL
hydrochloric acid (UNII: QTT17582CB)	
sodium hydroxide (UNII: 55X04QC32I)	
sucrose (UNII: C151H8M554)	94 mg in 1 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-9581-02	1 in 1 CARTON	12/19/2023	
1	NDC:0338-9581-01	10 mL in 1 VIAL, SINGLE-USE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
Unapproved drug for use in drug shortage		12/19/2023	

Labeler - Baxter Healthcare Corporation (005083209)

Revised: 12/2023 Baxter Healthcare Corporation