October 26, 2015

IMPORTANT PRESCRIBING INFORMATION

| Subject: | Availability of DOXIL® (doxorubicin HCl liposome injection) 50 mg in 30-mL vials |

Dear Healthcare Provider:

The purpose of this letter is to inform you of availability of DOXIL® 50 mg in 30-mL vials.

**Release of DOXIL® 50 mg vials**

Janssen is pleased to announce the availability of DOXIL® in both 20 mg and 50 mg vials. Janssen is committed to ensuring a long-term and reliable supply of DOXIL® through an approved manufacturing facility.

DOXIL® is available through normal distribution channels and can be ordered through your authorized distributor.

For ongoing updates, please visit [www.DOXIL.com](http://www.DOXIL.com) and [www.DOXILSupply.com](http://www.DOXILSupply.com).

**INDICATIONS**

DOXIL® is indicated for the treatment of patients with ovarian cancer whose disease has progressed or recurred after platinum-based chemotherapy.

DOXIL® is indicated for the treatment of AIDS-related Kaposi's sarcoma in patients after failure of prior systemic chemotherapy or intolerance to such therapy.

DOXIL® in combination with bortezomib is indicated for the treatment of patients with multiple myeloma who have not previously received bortezomib and have received at least one prior therapy.

**IMPORTANT SAFETY INFORMATION**

**CARDIOMYOPATHY and INFUSION-RELATED REACTIONS**

DOXIL® (doxorubicin HCl liposome injection) can cause myocardial damage, including congestive heart failure, as the total cumulative dose of doxorubicin HCl approaches 550 mg/m². In a clinical study of 250 patients with advanced cancer who were treated with DOXIL®, the risk of cardiotoxicity was 11% when the cumulative anthracycline dose was between 450-550 mg/m². Prior use of other anthracyclines or anthracenediones should be included in calculations of total cumulative dosage. The risk of cardiomyopathy may be increased at lower cumulative doses in patients with prior mediastinal irradiation. See additional information on Cardiomyopathy in Warnings and Precautions on following page.

*Please see Important Safety Information continued on page 2*

Please click here to see full [Prescribing Information](http://www-prescribinginformation.com) including BOXED WARNINGS.
IMPORTANT SAFETY INFORMATION (continued)

Acute infusion-related reactions consisting of, but not limited to, flushing, shortness of breath, facial swelling, headache, chills, back pain, tightness in the chest or throat, and/or hypotension occurred in 11% of patients with solid tumors treated with DOXIL® (doxorubicin HCl liposome injection). Serious, life-threatening and fatal infusion reactions have been reported. Medications/emergency equipment to treat such reactions should be available for immediate use. See additional information on Infusion-Related Reactions in Warnings and Precautions below.

Contraindications

DOXIL® is contraindicated in patients who have a history of severe hypersensitivity reactions, including anaphylaxis, to doxorubicin HCl.

Warnings and Precautions

Cardiomyopathy: Doxorubicin HCl can result in myocardial damage, including acute left ventricular failure. The risk of cardiomyopathy with doxorubicin HCl is generally proportional to the cumulative exposure. The relationship between cumulative DOXIL® dose and the risk of cardiac toxicity has not been determined. Assess left ventricular cardiac function (e.g. MUGA or echocardiogram) prior to initiation of DOXIL®, during treatment to detect acute changes, and after treatment to detect delayed cardiotoxicity. Administer DOXIL® to patients with a history of cardiovascular disease only when the potential benefit of treatment outweighs the risk.

Infusion-Related Reactions: Serious and sometimes life-threatening infusion-related reactions characterized by one or more of the following symptoms can occur with DOXIL®: flushing, shortness of breath, facial swelling, headache, chills, chest pain, back pain, tightness in the chest and throat, fever, tachycardia, pruritus, rash, cyanosis, syncope, bronchospasm, asthma, apnea, and hypotension. The majority of infusion-related events occurred during the first infusion. Ensure that medications to treat infusion-related reactions and cardiopulmonary resuscitative equipment is available for immediate use prior to initiation of DOXIL®. Initiate DOXIL® infusions at a rate of 1 mg/min and increase rate as tolerated.

In the event of an infusion-related reaction, temporarily stop the drug until resolution then resume at a reduced infusion rate. Discontinue DOXIL® infusion for serious or life-threatening infusion-related reactions.

Hand-foot syndrome (HFS): HFS may occur during therapy with DOXIL®. Based on HFS toxicity grade, dose reduction, delay in administration, or discontinuation of DOXIL® may be required.

- HFS was generally observed after 2 to 3 cycles of treatment, but may occur earlier
- Delay DOXIL® for the first episode of Grade 2 or greater HFS
- Discontinue DOXIL® if HFS is severe and debilitating

Secondary Oral Neoplasms: Cases of secondary oral cancer have been reported in patients with more than one year’s exposure to DOXIL®. Cases were diagnosed both during treatment and up to 6 years after the last dose. Patients should be examined at regular intervals for the presence of oral ulceration or any oral discomfort that may be indicative of secondary oral cancer.
Embryofetal Toxicity: Based on animal data, DOXIL® (doxorubicin HCl liposome injection) can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females and males of reproductive potential to use effective contraception during and for 6 months after treatment with DOXIL®.

Adverse Reactions
Most common adverse reactions observed with DOXIL® (>20%) are asthenia, fatigue, fever, anorexia, nausea, vomiting, stomatitis, diarrhea, constipation, hand-foot syndrome, rash, neutropenia, thrombocytopenia, and anemia.

Use in Specific Populations
• Lactation: Because of the potential for serious adverse reactions in nursing infants, discontinue nursing during treatment with DOXIL®.

Please see full Prescribing Information, including Boxed WARNINGS, for DOXIL® at www.DOXIL.com.

Reporting Adverse Events
Healthcare providers and patients are encouraged to report adverse events in patients taking DOXIL® to Janssen Medical Information at 1-800-JANSSEN (1-800-526-7736). You are also encouraged to report negative side effects of prescription drugs to the FDA either online, by regular mail or by fax:
  • Online: www.fda.gov/medwatch/report.htm
  • Regular mail: use postage-paid FDA form 3500 available at www.fda.gov/MedWatch/getforms.htm. Mail to: MedWatch, FDA, 5600 Fishers Lane, Rockville, MD 20852-9787
  • Fax: 1-800-FDA-0178

You may also contact our medical information department at 1-800-526-7736 if you have any questions about the information contained in this letter or the safe and effective use of DOXIL®

For additional information, please call Janssen Medical Information at 1-800-JANSSEN (1-800-526-7736) or visit www.DOXIL.com.

Sincerely,

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Janssen Products, LP