DOXORUBICIN

Differentiated Packaging on Vials and Cartons

Labels are DistinctIV™
- Easy-to-read drug name and strengths
- Unique label design to help distinguish DOXOrubicin from other drugs
- Tall Man labeling to help caregivers avoid confusion with drugs having look-alike names
- Available in both single- and multi-dose vials

Cartons are InformatIV™
- Full-color cartons that coordinate with the vial labels
- Distinctive label and cap color for each strength
- Cytotoxic agent caution on cartons and labels
- Preservative-free, AP rated, bar coded and not made with natural rubber latex

DOXOrubicin Hydrochloride Injection, USP

Please see full prescribing information, including boxed warning, for DOXOrubicin Hydrochloride Injection, USP, enclosed.
DOXOrubicin Hydrochloride Injection, USP

**Innovator Product Name: ADRIAMYCIN®**
(Adriamycin is a registered trademark of Pharmacia & Upjohn Company.)

<table>
<thead>
<tr>
<th>NDC Number</th>
<th>Description</th>
<th>Strength</th>
<th>Fill Volume</th>
<th>Concentration</th>
<th>Closure</th>
<th>Unit of Sale</th>
<th>Bar Coded</th>
</tr>
</thead>
<tbody>
<tr>
<td>25021-207-05</td>
<td>Glass Vial</td>
<td>10 mg</td>
<td>5 mL</td>
<td>2 mg per mL</td>
<td>20 mm</td>
<td>10 Vials</td>
<td>✔</td>
</tr>
<tr>
<td>25021-207-25</td>
<td>Glass Vial</td>
<td>50 mg</td>
<td>25 mL</td>
<td>2 mg per mL</td>
<td>20 mm</td>
<td>1 Vial</td>
<td>✔</td>
</tr>
<tr>
<td>25021-207-51</td>
<td>Glass Vial</td>
<td>200 mg</td>
<td>100 mL</td>
<td>2 mg per mL</td>
<td>20 mm</td>
<td>1 Vial</td>
<td>✔</td>
</tr>
</tbody>
</table>

This SAGENT product meets stringent FDA requirements and is AP rated, preservative-free and not made with natural rubber latex.

To order, or for more information about discovering Injectables Excellence™ with SAGENT, contact your sales representative, call 1-866-625-1618 or visit www.SagentPharma.com.

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**DOXOrubicin Hydrochloride Injection, USP**

**INDICATIONS AND USAGE**
Doxorubicin Hydrochloride Injection, USP is indicated:

- As a component of multi-agent adjuvant chemotherapy for treatment of women with axillary lymph node involvement following resection of primary breast cancer.

**IMPORTANT SAFETY INFORMATION**

**WARNING: CARDIOMYOPATHY, SECONDARY MALIGNANCES, EXTRAVASATION AND TISSUE NECROSIS, AND SEVERE MYELOSUPPRESSION**
- Cardiomyopathy: Myocardial damage, including acute left ventricular failure can occur with doxorubicin HCl. The risk of cardiomyopathy is proportional to the cumulative dose ranging from 300 mg/m² to 500 mg/m² when doxorubicin HCl is administered every 3 weeks. The risk of cardiomyopathy is further increased with concomitant cardiotoxic therapy. Assess LVEF before and regularly during and after treatment with doxorubicin HCl [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 doxorubicin HCl [see Warnings and Precautions (5.2)].
- Extravasation and Tissue Necrosis: Extravasation of doxorubicin HCl can result in severe local tissue injury and necrosis requiring wide excision of the affected area and skin grafting. Immediately terminate the drug and apply ice to the affected area [see Warnings and Precautions (5.3)].
- Severe myelosuppression resulting in serious infection, septic shock, requirement for transfusions, hospitalization, and death may occur [see Warnings and Precautions (5.4)].

**CONTRAINDICATIONS**
Doxorubicin HCl is contraindicated in patients with:

- Severe myocardial insufficiency
- Recent (occurring within the past 4 to 6 weeks) myocardial infarction
- Severe persistent drug-induced myelosuppression
- Severe hepatic impairment (defined as Child Pugh Class C or serum bilirubin level greater than 5 mg/dL)
- Severe hypersensitivity reaction to doxorubicin HCl including anaphylaxis

**WARNINGS AND PRECAUTIONS**
- Radiation-induced toxicity can be increased by the administration of doxorubicin HCl. Radiation recall can occur in patients who receive doxorubicin HCl after prior radiation therapy.
- Embryofetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of potential risk to the fetus.

**ADVERSE REACTIONS**
The most common (>10%) adverse drug reactions are alopecia, nausea and vomiting.

**DRUG INTERACTIONS**
- Avoid concurrent use of doxorubicin HCl with inhibitors and inducers of CYP3A4, CYP2D6, and/or P-gp.
- Do not administer doxorubicin HCl in combination with trastuzumab due to increased risk of cardiac dysfunction.

**USE IN SPECIFIC POPULATIONS**
- Nursing Mothers: Discontinue drug or nursing taking into consideration importance of drug to mother.
- Pediatric Use: Recommend long-term follow-up cardiac evaluations due to risk of delayed cardiotoxicity.
- Females and Males of Reproductive Potential: May impair fertility. Counsel female and male patients on pregnancy planning and prevention.

**OVERDOSAGE**
Acute overdosage with doxorubicin enhances the toxic effect of mucositis, leukopenia, and thrombocytopenia. Treatment of acute overdosage consists of treatment of the severely myelosuppressed patient.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088

Please see full prescribing information for DOXOrubicin Hydrochloride Injection, USP.

Doxorubicin Hydrochloride Injection, USP, may contain 10 mg/mL, 50 mg/mL, or 200 mg/mL per 2 mL, and 200 mg/mL per 4 mL, as a solution. (5)

CONTRAINDICATIONS

• Severe myocardial infarct (4)
• Recent myocardial infarct (4)
• Severe persistent drug-induced myelosuppression (4)
• Severe hepatic impairment (4)
• Hypersensitivity to doxorubicin HCl (4)

WARNINGS AND PRECAUTIONS

• Radiation-induced toxicity can be increased by the administration of doxorubicin HCl. Radiation recall can occur in patients who receive doxorubicin HCl after prior radiation therapy (5.7).
• Embryofetal Toxicity: Can cause fetal harm when administered to pregnant women. (5.8)

ADVERSE REACTIONS

The most common (>10%) adverse drug reactions are alopecia, nausea, and vomiting (5.1). To report SUSPECTED ADVERSE REACTIONS, contact Saget Pharmaceuticals, Inc. at 1-888-625-1816 or FDA at 1-800-FDA-1234 or www.fda.gov/medwatch.

DOSE INTERACTIONS

Avoid concurrent use of doxorubicin HCl and interferon- 

USE IN SPECIFIC POPULATIONS

• Nursing Mothers: Doxorubicin or drug-taking into consideration importance of drug to mother (5.3).
• Pediatric Use: Recommended long-term follow-up cardiac evaluations due to risk of delayed cardiomyopathy (5.7).
• Females and Males of Reproductive Potential: May impair fertility. Counsel female and male patients on pregnancy planning and potential effects on the fetus (5.8).

See 17 FOR PATIENT COUNSELING INFORMATION AND FDA-approved patient labeling.

Revised: 01/04

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Doxorubicin Hydrochloride Injection, USP is contraindicated in patients who are hypersensitive to doxorubicin, doxorubicin HCl, or any of the excipients in the formulation.

4. WARNINGS AND PRECAUTIONS

4.1 General

Cardiovascular

Cardiovascular toxicity is a major dose limiting factor. The risk of cardiovascular toxicity is increased in patients with prior anthracycline exposure or those receiving doses greater than 500 mg/m².

Cardiovascular events such as congestive heart failure, cardiac dysfunction, stellate ganglion syndrome, and pericardial effusion may occur during treatment or within 2 years of the completion of treatment with doxorubicin hydrochloride injection. Cardiotoxicity may develop during treatment or up to several years after completion of treatment, with an increasing incidence over time. This risk appears to be dose dependent with cumulative doses greater than 450 mg/m² associated with a higher risk of symptomatic cardiomyopathy or congestive heart failure. (5.1)

Heart failure

Doxorubicin may cause heart muscle damage that may lead to congestive heart failure. This condition occurs more often in women than in men. Doxorubicin may cause heart muscle damage in women at a lower cumulative dose when compared to men. Heart failure may be irreversible in some cases and can lead to death. Heart failure can happen during your treatment with Doxorubicin or after stopping treatment. Your risk of heart muscle damage increases with higher total amounts of doxorubicin hydrochloride that you receive in your lifetime. Your risk of heart failure is higher if you:
• have already had heart problems
• have needed radiation therapy to your chest
• have had treatment with other anti-cancer medicines
• have other medicines that can have serious side effects on your heart

Tell your doctor if you get any of these symptoms of heart failure during or after treatment with Doxorubicin:

• extreme fatigue or weakness
• fast heartbeat
• shortness of breath
• swelling of your feet and ankles

Doxorubicin is a prescription medicine used to treat certain types of cancers. Doxorubicin should not be used alone or in combination with other prescription medicines. (4)

4.2 Skin

Skin damage near the vein where Doxorubicin is given (injection site reactions)

Doxorubicin can cause damage to the skin. It can cause pain and swelling. (5.2)

Skin reactions include pain, redness, and swelling at the site of injection.

Doxorubicin is a prescription medicine used to treat certain types of cancers. Doxorubicin should not be used alone or in combination with other prescription medicines. (4)

4.3 Infections

Doxorubicin may increase the risk of developing certain infections called acute myelogenous leukemia (AML) or myelodysplastic syndrome (MDS) after treatment with doxorubicin. Tell your doctor right away if you get a fever (temperature of 100°F [38°C] or higher) or chills with swelling. (5.3)

Doxorubicin is a prescription medicine used to treat certain types of cancers. Doxorubicin should not be used alone or in combination with other prescription medicines. (4)

4.4 Skin Cancer

Doxorubicin is a prescription medicine used to treat certain types of cancers. Doxorubicin should not be used alone or in combination with other prescription medicines. (4)

4.5 Gastrointestinal

Doxorubicin is a prescription medicine used to treat certain types of cancers. Doxorubicin should not be used alone or in combination with other prescription medicines. (4)
Doxorubicin HCl may cause infertility in males and females of reproductive potential. Consult information on fertility before therapy. Consult information on contraception before starting therapy. Consult information on pregnancy before starting therapy. Consult information on breastfeeding before starting therapy. Consult information on fertility before stopping therapy. Consult information on contraception before stopping therapy. Consult information on pregnancy before stopping therapy. Consult information on breastfeeding before stopping therapy. Consult information on fertility after stopping therapy. Consult information on contraception after stopping therapy. Consult information on pregnancy after stopping therapy. Consult information on breastfeeding after stopping therapy. Consult information on fertility before treatment. Consult information on contraception before treatment. Consult information on pregnancy before treatment. Consult information on breastfeeding before treatment. Consult information on fertility after treatment. Consult information on contraception after treatment. Consult information on pregnancy after treatment. Consult information on breastfeeding after treatment.

Isotretinoin is a teratogen. In women of childbearing potential, doxorubicin HCl may potentiate the teratogenic and embryotoxic effects of isotretinoin. Use of an effective contraceptive is recommended during and for 6 months after treatment with doxorubicin HCl. Use of an effective contraceptive is recommended during and for 6 months after treatment with isotretinoin. Otherwise, patients should be advised to use a barrier method of contraception (condoms) during and for 6 months after treatment with doxorubicin HCl and for 6 months after treatment with isotretinoin. Use of an effective contraceptive is recommended during and for 6 months after treatment with doxorubicin HCl. The simultaneous use of isotretinoin and doxorubicin HCl is contraindicated.

Other aspects of specificity to doxorubicin HCl are not discussed in detail, but it is known to be a tumor-selective agent, to be more active in tumor than normal tissues, and to be more active in chemically induced than naturally occurring tumors. It is currently being used in the treatment of a wide variety of tumors, including those of the breast, ovary, lung, and brain. The mechanism of action of doxorubicin HCl is unknown, but it is thought to be related to the inhibition of DNA synthesis and repair.

**REGISTRATION**

Doxorubicin HCl is registered for the treatment of cancer in the United States by the Food and Drug Administration (FDA) and by the European Union (E.U.) as a part of the European Medicines Agency (EMA) marketing authorization. In the United States, doxorubicin HCl is approved for the treatment of cancer in the United States by the FDA as a part of the EMA marketing authorization.

**PHARMACOKINETICS**

Doxorubicin HCl is administered intravenously as a solution of doxorubicin hydrochloride in water for injection. Doxorubicin HCl is rapidly absorbed from the intravenous injection site. Doxorubicin HCl is rapidly distributed to the extracellular fluid and to muscles. Doxorubicin HCl is excreted primarily in the urine, with a small amount excreted in the feces.

**INDICATIONS AND USAGE**

Doxorubicin HCl is indicated for the treatment of patients with advanced breast cancer who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced ovarian cancer who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent non-small cell lung cancer who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent head and neck cancer who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent esophageal cancer who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent cervical cancer who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent gastrointestinal cancer who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent genitourinary cancer who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent hematologic malignancies who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent non-Hodgkin lymphoma who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent Hodgkin lymphoma who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent soft tissue sarcoma who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent head and neck cancer who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent esophageal cancer who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent cervical cancer who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent gastrointestinal cancer who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent genitourinary cancer who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent hematologic malignancies who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent non-Hodgkin lymphoma who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent Hodgkin lymphoma who have relapsed following initial therapy. Doxorubicin HCl is also indicated for the treatment of patients with advanced or recurrent soft tissue sarcoma who have relapsed following initial therapy.