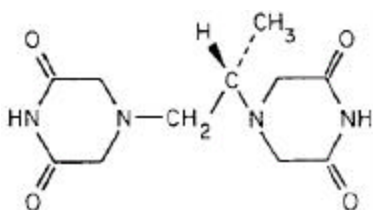


1  
2 **Zinecard<sup>®</sup>**  
3 **dexrazoxane for injection**

4  
5  
6 **DESCRIPTION**

7  
8 ZINECARD<sup>®</sup> (dexrazoxane for injection) is a sterile, pyrogen-free lyophilizate intended for  
9 intravenous administration. It is a cardioprotective agent for use in conjunction with doxorubicin.

10  
11 Chemically, dexrazoxane is (S)-4,4'-(1-methyl-1,2-ethanediyl)bis-2,6-piperazinedione. The structural  
12 formula is as follows:



13  
14  $C_{11}H_{16}N_4O_4$  M.W. 268.28

15  
16 Dexrazoxane, a potent intracellular chelating agent is a derivative of EDTA. Dexrazoxane is a whitish  
17 crystalline powder which melts at 191° to 197°C. It is sparingly soluble in water and 0.1 N HCl,  
18 slightly soluble in ethanol and methanol and practically insoluble in nonpolar organic solvents. The  
19  $pK_a$  is 2.1. Dexrazoxane has an octanol/water partition coefficient of 0.025 and degrades rapidly  
20 above a pH of 7.0.

21  
22 ZINECARD is available in 250 mg and 500 mg single use only vials.

23 Each **250 mg vial** contains dexrazoxane hydrochloride equivalent to 250 mg dexrazoxane.

24 Hydrochloric Acid, NF is added for pH adjustment. When reconstituted as directed with the 25  
25 mL vial of 0.167 Molar (M/6) Sodium Lactate Injection, USP diluent provided, each mL  
26 contains: 10 mg dexrazoxane. The pH of the resultant solution is 3.5 to 5.5.

27 Each **500 mg vial** contains dexrazoxane hydrochloride equivalent to 500 mg dexrazoxane.

28 Hydrochloric Acid, NF is added for pH adjustment. When reconstituted as directed with the 50  
29 mL vial of 0.167 Molar (M/6) Sodium Lactate Injection, USP diluent provided, each mL  
30 contains: 10 mg dexrazoxane. The pH of the resultant solution is 3.5 to 5.5.

31  
32 **CLINICAL PHARMACOLOGY**

33  
34 **Mechanism of Action:** The mechanism by which ZINECARD exerts its cardioprotective activity is  
35 not fully understood. Dexrazoxane is a cyclic derivative of EDTA that readily penetrates cell  
36 membranes. Results of laboratory studies suggest that dexrazoxane is converted intracellularly to a  
37 ring-opened chelating agent that interferes with iron-mediated free radical generation thought to be  
38 responsible, in part, for anthracycline-induced cardiomyopathy.

39  
40 **Pharmacokinetics:** The pharmacokinetics of dexrazoxane have been studied in advanced cancer  
41 patients with normal renal and hepatic function. Generally, the pharmacokinetics of dexrazoxane can  
42 be adequately described by a two-compartment open model with first-order elimination. Dexrazoxane  
43 has been administered as a 15 minute infusion over a dose-range of 60 to 900 mg/m<sup>2</sup> with 60 mg/m<sup>2</sup>  
44 of doxorubicin, and at a fixed dose of 500 mg/m<sup>2</sup> with 50 mg/m<sup>2</sup> doxorubicin. The disposition  
45 kinetics of dexrazoxane are dose-independent, as shown by linear relationship between the area under

46 plasma concentration-time curves and administered doses ranging from 60 to 900 mg/m<sup>2</sup>. The mean  
 47 peak plasma concentration of dexrazoxane was 36.5 µg/mL at the end of the 15 minute infusion of a  
 48 500 mg/m<sup>2</sup> dose of ZINECARD administered 15 to 30 minutes prior to the 50 mg/m<sup>2</sup> doxorubicin  
 49 dose. The important pharmacokinetic parameters of dexrazoxane are summarized in the following  
 50 table.

51 SUMMARY OF MEAN (% CV<sup>a</sup>) DEXRAZOXANE  
 52 PHARMACOKINETIC PARAMETERS AT A DOSAGE RATIO OF  
 53 10:1 OF ZINECARD: DOXORUBICIN  
 54

Dose Doxorubicin (mg/m <sup>2</sup> )	Dose Zinecard (mg/m <sup>2</sup> )	Number of Subjects	Elimination Half-Life (h)	Plasma Clearance (L/h/m <sup>2</sup> )	Renal Clearance (L/h/m <sup>2</sup> )	<sup>b</sup> Volume of Distribution (L/m <sup>2</sup> )
50	500	10	2.5 (16)	7.88 (18)	3.35 (36)	22.4 (22)
60	600	5	2.1 (29)	6.25 (31)	—	22.0 (55)

55 <sup>a</sup> Coefficient of variation

56 <sup>b</sup> Steady-state volume of distribution

57  
 58 Following a rapid distributive phase (~0.2 to 0.3 hours), dexrazoxane reaches postdistributive  
 59 equilibrium within two to four hours. The estimated steady-state volume of distribution of  
 60 dexrazoxane suggests its distribution primarily in the total body water (25 L/m<sup>2</sup>). The mean systemic  
 61 clearance and steady-state volume of distribution of dexrazoxane in two Asian female patients at 500  
 62 mg/m<sup>2</sup> dexrazoxane along with 50mg/m<sup>2</sup> doxorubicin were 15.15 L/h/m<sup>2</sup> and 36.27 L/m<sup>2</sup>,  
 63 respectively, but their elimination half-life and renal clearance of dexrazoxane were similar to those  
 64 of the ten Caucasian patients from the same study. Qualitative metabolism studies with ZINECARD  
 65 have confirmed the presence of unchanged drug, a diacid-diamide cleavage product, and two  
 66 monoacid-monoamide ring products in the urine of animals and man. The metabolite levels were not  
 67 measured in the pharmacokinetic studies.

68  
 69 Urinary excretion plays an important role in the elimination of dexrazoxane. Forty-two percent of the  
 70 500 mg/m<sup>2</sup> dose of ZINECARD was excreted in the urine.

71  
 72 Protein Binding: *In vitro* studies have shown that ZINECARD is not bound to plasma proteins.

73  
 74 **Special Populations:**

75 Pediatric: The pharmacokinetics of ZINECARD have not been evaluated in pediatric patients.

76 Gender: Analysis of pooled data from two pharmacokinetic studies indicate that male patients have a  
 77 lower mean clearance value than female patients (110 ml/min/m<sup>2</sup> versus 133 ml/min/m<sup>2</sup>). This gender  
 78 effect is not clinically relevant.

79 Renal insufficiency: The pharmacokinetics of ZINECARD have not been evaluated in patients with  
 80 renal impairment.

81 Hepatic insufficiency: The pharmacokinetics of ZINECARD have not been evaluated in patients with  
 82 hepatic impairment. The ZINECARD dose is dependent upon the dose of doxorubicin (see Dosage  
 83 and Administration). Since a doxorubicin dose reduction is recommended in the presence of  
 84 hyperbilirubinemia, the ZINECARD dosage is proportionately reduced in patients with hepatic  
 85 impairment.

86 **Drug Interactions:** There was no significant change in the pharmacokinetics of doxorubicin (50  
 87 mg/m<sup>2</sup>) and its predominant metabolite, doxorubicinol, in the presence of dexrazoxane (500 mg/m<sup>2</sup>)  
 88 in a crossover study in cancer patients.

89  
 90

91 **CLINICAL STUDIES**

92  
93 The ability of ZINECARD to prevent/reduce the incidence and severity of doxorubicin-induced  
94 cardiomyopathy was demonstrated in three prospectively randomized placebo-controlled studies. In  
95 these studies, patients were treated with a doxorubicin-containing regimen and either ZINECARD or  
96 placebo starting with the first course of chemotherapy. There was no restriction on the cumulative  
97 dose of doxorubicin. Cardiac function was assessed by measurement of the left ventricular ejection  
98 fraction (LVEF), utilizing resting multigated nuclear medicine (MUGA) scans, and by clinical  
99 evaluations. Patients receiving ZINECARD had significantly smaller mean decreases from baseline in  
100 LVEF and lower incidences of congestive heart failure than the control group. The difference in  
101 decline from baseline in LVEF was evident beginning with a cumulative doxorubicin dose of 150  
102 mg/m<sup>2</sup> and reached statistical significance in patients who received ≥400 mg/m<sup>2</sup> of doxorubicin. In  
103 addition to evaluating the effect of ZINECARD on cardiac function, the studies also assessed the  
104 effect of the addition of ZINECARD on the anti-tumor efficacy of the chemotherapy regimens. In one  
105 study (the largest of three breast cancer studies) patients with advanced breast cancer receiving  
106 fluorouracil, doxorubicin and cyclophosphamide (FAC) with ZINECARD had a lower response rate  
107 (48% vs 63%; p=0.007) and a shorter time to progression than patients who received FAC + placebo,  
108 although the survival of patients who did or did not receive ZINECARD with FAC was similar.  
109

110 Two of the randomized breast cancer studies evaluating the efficacy and safety of FAC with either  
111 ZINECARD or placebo were amended to allow patients on the placebo arm who had attained a  
112 cumulative dose of doxorubicin of 300 mg/m<sup>2</sup> (six courses of FAC) to receive FAC with open-label  
113 ZINECARD for each subsequent course. This change in design allowed examination of whether there  
114 was a cardioprotective effect of ZINECARD even when it was started after substantial exposure to  
115 doxorubicin.  
116

117 Retrospective historical analyses were then performed to compare the likelihood of heart failure in  
118 patients to whom ZINECARD was added to the FAC regimen after they had received six (6) courses  
119 of FAC (and who then continued treatment with FAC therapy) with the heart failure rate in patients  
120 who had received six (6) courses of FAC and continued to receive this regimen without added  
121 ZINECARD. These analyses showed that the risk of experiencing a cardiac event (see Table 1 for  
122 definition) at a given cumulative dose of doxorubicin above 300 mg/m<sup>2</sup> was substantially greater in  
123 the 99 patients who did not receive ZINECARD beginning with their seventh course of FAC than in  
124 the 102 patients who did receive ZINECARD (See Figure 1).  
125

126 **Table 1**

127 **The development of cardiac events is shown by:**

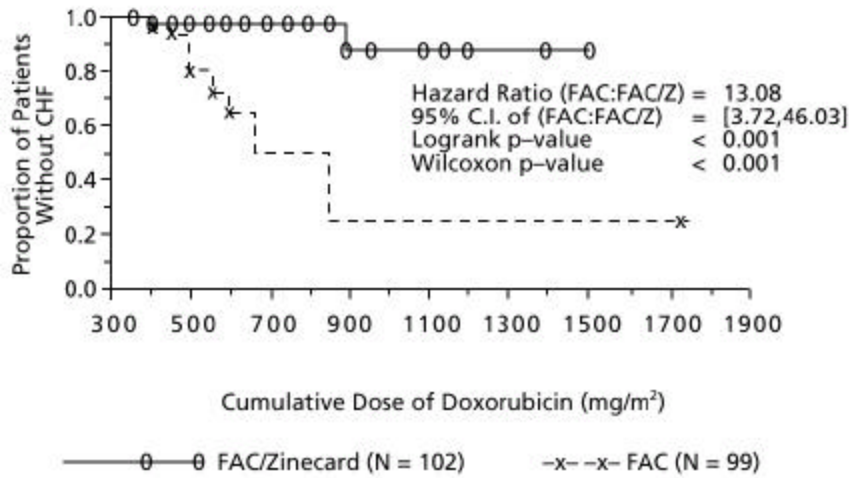
- 128 1. Development of congestive heart failure, defined as having two or more of the following:  
129 a. Cardiomegaly by X-ray  
130 b. Basilar Rales  
131 c. S<sub>3</sub> Gallop  
132 d. Paroxysmal nocturnal dyspnea and/or orthopnea and/or significant dyspnea on exertion.  
133 2. Decline from baseline in LVEF by ≥10% and to below the lower limit of normal for the  
134 institution.  
135 3. Decline in LVEF by ≥20% from baseline value.  
136 4. Decline in LVEF to ≥5% below lower limit of normal for the institution.  
137

138 Figure 1 displays the risk of developing congestive heart failure by cumulative dose of doxorubicin in  
139 patients who received ZINECARD starting with their seventh course of FAC compared to patients  
140 who did not. Patients unprotected by ZINECARD had a 13 times greater risk of developing

141 congestive heart failure. Overall, 3% of patients treated with ZINECARD developed CHF compared  
 142 with 22% of patients not receiving ZINECARD.

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 144  
 145  
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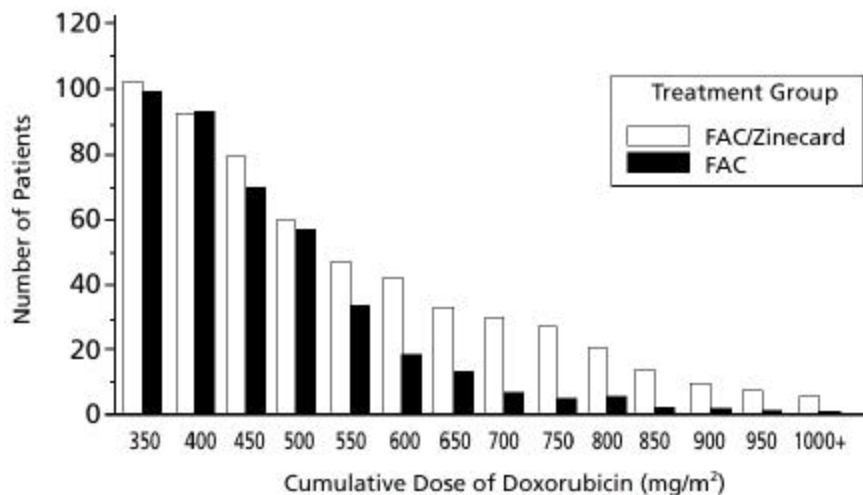
**Figure 1**  
**Doxorubicin Dose at Congestive Heart Failure (CHF)**  
**FAC vs. FAC/ZINECARD Patients**  
**Patients Receiving At Least Seven Courses of Treatment**



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Because of its cardioprotective effect, ZINECARD permitted a greater percentage of patients to be treated with extended doxorubicin therapy. Figure 2 shows the number of patients still on treatment at increasing cumulative doses.

**Figure 2**  
**Cumulative Number of Patients On Treatment**  
**FAC vs. FAC/ZINECARD Patients**  
**Patients Receiving At Least Seven Courses of Treatment**



158  
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 163

In addition to evaluating the cardioprotective efficacy of ZINECARD in this setting, the time to tumor progression and survival of these two groups of patients were also compared. There was a similar time to progression in the two groups and survival was at least as long for the group of patients that received ZINECARD starting with their seventh course, i.e., starting after a cumulative

164 dose of doxorubicin of 300 mg/m<sup>2</sup>. These time to progression and survival data should be interpreted  
165 with caution, however, because they are based on comparisons of groups entered sequentially in the  
166 studies and are not comparisons of prospectively randomized patients.  
167

## 168 169 **INDICATIONS AND USAGE**

170  
171 ZINECARD is indicated for reducing the incidence and severity of cardiomyopathy associated with  
172 doxorubicin administration in women with metastatic breast cancer who have received a cumulative  
173 doxorubicin dose of 300 mg/m<sup>2</sup> and who will continue to receive doxorubicin therapy to maintain  
174 tumor control. It is not recommended for use with the initiation of doxorubicin therapy (see  
175 WARNINGS).  
176

## 177 **CONTRAINDICATIONS**

178  
179 ZINECARD should not be used with chemotherapy regimens that do not contain an anthracycline.  
180

## 181 182 **WARNINGS**

183  
184 ZINECARD may add to the myelosuppression caused by chemotherapeutic agents.  
185

186 There is some evidence that the use of dexrazoxane concurrently with the initiation of fluorouracil,  
187 doxorubicin and cyclophosphamide (FAC) therapy interferes with the antitumor efficacy of the  
188 regimen, and this use is not recommended. In the largest of three breast cancer trials, patients who  
189 received dexrazoxane starting with their first cycle of FAC therapy had a lower response rate (48% vs  
190 63%; p=0.007) and shorter time to progression than patients who did not receive dexrazoxane (see  
191 **Clinical Studies** section of **CLINICAL PHARMACOLOGY**). Therefore, ZINECARD should only  
192 be used in those patients who have received a cumulative doxorubicin dose of 300 mg/m<sup>2</sup> and are  
193 continuing with doxorubicin therapy.  
194

195 Although clinical studies have shown that patients receiving FAC with ZINECARD may receive a  
196 higher cumulative dose of doxorubicin before experiencing cardiac toxicity than patients receiving  
197 FAC without ZINECARD, the use of ZINECARD in patients who have already received a  
198 cumulative dose of doxorubicin of 300 mg/m<sup>2</sup> without ZINECARD, does not eliminate the potential  
199 for anthracycline induced cardiac toxicity. Therefore, cardiac function should be carefully monitored.  
200

201 Secondary malignancies (primarily acute myeloid leukemia) have been reported in patients treated  
202 chronically with oral razoxane. Razoxane is the racemic mixture, of which dexrazoxane is the S(+)-  
203 enantiomer. In these patients, the total cumulative dose of razoxane ranged from 26 to 480 grams and  
204 the duration of treatment was from 42 to 319 weeks. One case of T-cell lymphoma, a case of B-cell  
205 lymphoma and six to eight cases of cutaneous basal cell or squamous cell carcinoma have also been  
206 reported in patients treated with razoxane.  
207

## 208 209 **PRECAUTIONS**

### 210 211 **General**

212  
213 Doxorubicin should not be given prior to the intravenous injection of ZINECARD. ZINECARD  
214 should be given by slow I.V. push or rapid drip intravenous infusion from a bag. Doxorubicin should

215 be given within 30 minutes after beginning the infusion with ZINECARD. (See **DOSAGE AND**  
216 **ADMINISTRATION**).

217  
218 As ZINECARD will always be used with cytotoxic drugs, patients should be monitored closely.  
219 While the myelosuppressive effects of ZINECARD at the recommended dose are mild, additive  
220 effects upon the myelosuppressive activity of chemotherapeutic agents may occur.

221  
222 **Laboratory tests**

223  
224 As ZINECARD may add to the myelosuppressive effects of cytotoxic drugs, frequent complete blood  
225 counts are recommended. (See **ADVERSE REACTIONS**).

226  
227 **Drug Interactions**

228  
229 ZINECARD does not influence the pharmacokinetics of doxorubicin.

230  
231 **Carcinogenesis, Mutagenesis, Impairment of Fertility** (see **WARNINGS** section for information  
232 on human carcinogenicity)

233  
234 No long-term carcinogenicity studies have been carried out with dexrazoxane in animals.  
235 Dexrazoxane was not mutagenic in the Ames test but was found to be clastogenic to human  
236 lymphocytes in vitro and to mouse bone marrow erythrocytes in vivo (micronucleus test).

237  
238 The possible adverse effects of ZINECARD on the fertility of humans and experimental animals,  
239 male or female, have not been adequately studied. Testicular atrophy was seen with dexrazoxane  
240 administration at doses as low as 30 mg/kg weekly for 6 weeks in rats (1/3 the human dose on a  
241 mg/m<sup>2</sup> basis) and as low as 20 mg/kg weekly for 13 weeks in dogs (approximately equal to the human  
242 dose on a mg/m<sup>2</sup> basis).

243  
244 **Pregnancy - Pregnancy Category C**

245  
246 Dexrazoxane was maternotoxic at doses of 2 mg/kg (1/40 the human dose on a mg/m<sup>2</sup> basis) and  
247 embryotoxic and teratogenic at 8 mg/kg (approximately 1/10 the human dose on a mg/m<sup>2</sup> basis) when  
248 given daily to pregnant rats during the period of organogenesis. Teratogenic effects in the rat included  
249 imperforate anus, microphthalmia, and anophthalmia. In offspring allowed to develop to maturity,  
250 fertility was impaired in the male and female rats treated in utero during organogenesis at 8 mg/kg. In  
251 rabbits, doses of 5 mg/kg (approximately 1/10 the human dose on a mg/m<sup>2</sup> basis) daily during the  
252 period of organogenesis were maternotoxic and dosages of 20 mg/kg (1/2 the human dose on a mg/m<sup>2</sup>  
253 basis) were embryotoxic and teratogenic. Teratogenic effects in the rabbit included several skeletal  
254 malformations such as short tail, rib and thoracic malformations, and soft tissue variations including  
255 subcutaneous, eye and cardiac hemorrhagic areas, as well as agenesis of the gallbladder and of the  
256 intermediate lobe of the lung. There are no adequate and well-controlled studies in pregnant women.  
257 ZINECARD should be used during pregnancy only if the potential benefit justifies the potential risk  
258 to the fetus.

259  
260 **Nursing Mothers**

261  
262 It is not known whether dexrazoxane is excreted in human milk. Because many drugs are excreted in  
263 human milk and because of the potential for serious adverse reactions in nursing infants exposed to  
264 dexrazoxane, mothers should be advised to discontinue nursing during dexrazoxane therapy.

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**Pediatric Use**

Safety and effectiveness of dexrazoxane in pediatric patients have not been established.

**Geriatric Use**

Clinical studies of ZINECARD did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, elderly patients should be treated with caution due to the greater frequency of decreased hepatic, renal, or cardiac function, and concomitant disease or other drug therapy.

**ADVERSE REACTIONS**

ZINECARD at a dose of 500 mg/m<sup>2</sup> has been administered in combination with FAC in randomized, placebo-controlled, double-blind studies to patients with metastatic breast cancer. The dose of doxorubicin was 50 mg/m<sup>2</sup> in each of the trials. Courses were repeated every three weeks, provided recovery from toxicity had occurred. Table 2 below lists the incidence of adverse experiences for patients receiving FAC with either ZINECARD or placebo in the breast cancer studies. Adverse experiences occurring during courses 1 through 6 are displayed for patients receiving ZINECARD or placebo with FAC beginning with their first course of therapy (column 1 & 3, respectively). Adverse experiences occurring at course 7 and beyond for patients who received placebo with FAC during the first six courses and who then received either ZINECARD or placebo with FAC are also displayed (column 2 & 4, respectively).

**Table 2**

ADVERSE EXPERIENCE	PERCENTAGE (%) OF BREAST CANCER PATIENTS WITH ADVERSE EXPERIENCE			
	FAC + ZINECARD		FAC + PLACEBO	
	Courses 1-6 N = 413	Courses ≥ 7 N = 102	Courses 1-6 N = 458	Course ≥ 7 N = 99
Alopecia	94	100	97	98
Nausea	77	51	84	60
Vomiting	59	42	72	49
Fatigue/Malaise	61	48	58	55
Anorexia	42	27	47	38
Stomatitis	34	26	41	28
Fever	34	22	29	18
Infection	23	19	18	21
Diarrhea	21	14	24	7
Pain on Injection	12	13	3	0
Sepsis	17	12	14	9
Neurotoxicity	17	10	13	5
Streaking/Erythema	5	4	4	2
Phlebitis	6	3	3	5
Esophagitis	6	3	7	4
Dysphagia	8	0	10	5
Hemorrhage	2	3	2	1
Extravasation	1	3	1	2
Urticaria	2	2	2	0
Recall Skin Reaction	1	1	2	0

292

293 The adverse experiences listed above are likely attributable to the FAC regimen with the exception of  
294 pain on injection that was observed mainly on the ZINECARD arm.

295

### 296 Myelosuppression

297 Patients receiving FAC with ZINECARD experienced more severe leucopenia, granulocytopenia and  
298 thrombocytopenia at nadir than patients receiving FAC without ZINECARD, but recovery counts  
299 were similar for the two groups of patients.

300

### 301 Hepatic and Renal

302 Some patients receiving FAC + ZINECARD or FAC + placebo experienced marked abnormalities in  
303 hepatic or renal function tests, but the frequency and severity of abnormalities in bilirubin, alkaline  
304 phosphatase, BUN, and creatinine were similar for patients receiving FAC with or without  
305 ZINECARD.

306

307

## 308 **OVERDOSAGE**

309

310 There have been no instances of drug overdose in the clinical studies sponsored by either Pharmacia  
311 & Upjohn Company or the National Cancer Institute. The maximum dose administered during the  
312 cardioprotective trials was 1000 mg/m<sup>2</sup> every three weeks.

313

314 Disposition studies with ZINECARD have not been conducted in cancer patients undergoing dialysis,  
315 but retention of a significant dose fraction (>0.4) of the unchanged drug in the plasma pool, minimal  
316 tissue partitioning or binding, and availability of greater than 90% of the systemic drug levels in the  
317 unbound form suggest that it could be removed using conventional peritoneal or hemodialysis.

318

319 There is no known antidote for dexrazoxane. Instances of suspected overdose should be managed  
320 with good supportive care until resolution of myelosuppression and related conditions is complete.  
321 Management of overdose should include treatment of infections, fluid regulation, and maintenance of  
322 nutritional requirements.

323

324

## 325 **DOSAGE AND ADMINISTRATION**

326

327 The recommended dosage ratio of ZINECARD:doxorubicin is 10:1 (eg, 500 mg/m<sup>2</sup> ZINECARD:50  
328 mg/m<sup>2</sup> doxorubicin). Since a doxorubicin dose reduction is recommended in the presence of  
329 hyperbilirubinemia, the ZINECARD dosage should be proportionately reduced (maintaining the 10:1  
330 ratio) in patients with hepatic impairment. ZINECARD must be reconstituted with 0.167 Molar (M/6)  
331 Sodium Lactate Injection, USP, to give a concentration of 10 mg ZINECARD for each mL of sodium  
332 lactate. The reconstituted solution should be given by slow I.V. push or rapid drip intravenous  
333 infusion from a bag. After completing the infusion of ZINECARD, and prior to a total elapsed time of  
334 30 minutes (from the beginning of the ZINECARD infusion), the intravenous injection of  
335 doxorubicin should be given.

336

337 Reconstituted ZINECARD, when transferred to an empty infusion bag, is stable for 6 hours from the  
338 time of reconstitution when stored at controlled room temperature, 15° to 30°C (59° to 86°F) or under  
339 refrigeration, 2° to 8°C (36° to 46°F). DISCARD UNUSED SOLUTIONS.

340

341 The reconstituted ZINECARD solution may be diluted with either 0.9% Sodium Chloride Injection,  
342 USP or 5.0% Dextrose Injection, USP to a concentration range of 1.3 to 5.0 mg/mL in intravenous



343 infusion bags. The resultant solutions are stable for 6 hours when stored at controlled room  
344 temperature, 15° to 30°C (59° to 86°F) or under refrigeration, 2° to 8°C (36° to 46°F). DISCARD  
345 UNUSED SOLUTIONS.

346

### 347 **Incompatibility**

348

349 ZINECARD should not be mixed with other drugs.

350

351 Parenteral drug products should be inspected visually for particulate matter and discoloration prior to  
352 administration, whenever solution and container permit.

353

354 **Handling and Disposal:** Caution in the handling and preparation of the reconstituted solution must  
355 be exercised and the use of gloves is recommended. If ZINECARD powder or solutions contact the  
356 skin or mucosae, immediately wash thoroughly with soap and water.

357

358 Procedures normally used for proper handling and disposal of anti-cancer drugs should be considered  
359 for use with ZINECARD. Several guidelines on this subject have been published.<sup>1-7</sup> There is no  
360 general agreement that all of the procedures recommended in the guidelines are necessary or  
361 appropriate.

362

363

### 364 **HOW SUPPLIED**

365

366 ZINECARD® (dexrazoxane for injection) is available in the following strengths as sterile, pyrogen-  
367 free lyophilizates.

368

369 NDC 0013-8715-62 250 mg single dose vial with a red  
370 flip-top seal, packaged in single vial packs.  
371 (This package also contains a 25 mL vial of 0.167 Molar (M/6) Sodium Lactate Injection, USP.)

372

373 NDC 0013-8725-89 500 mg single dose vial with a blue  
374 flip-top seal, packaged in single vial packs.  
375 (This package also contains a 50 mL vial of 0.167 Molar (M/6) Sodium Lactate Injection, USP.)

376

377 Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room  
378 Temperature]. Reconstituted solutions of ZINECARD are stable for 6 hours at controlled room  
379 temperature or under refrigeration, 2° to 8°C (36° to 46°F). DISCARD UNUSED SOLUTIONS.

380

### 381 **Rx only**

382

383

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413  
414

415 Manufactured for: Pharmacia & Upjohn Company  
416 Kalamazoo, MI 49001, USA  
417 By: SP Pharmaceuticals LLC  
418 Albuquerque, NM 87109, USA  
419

420 August 1998

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