

## Temperature- and Volume-dependent Dissolution of Amifostine 500mg Reconstituted for Subcutaneous Injection in Normal Saline or Sterile Water for Injection [3207]

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**Background:** Because the dissolution of amifostine (Ethyol) 500 mg in 0.9% normal saline (NaCl) or sterile water for injection (SWI) for subcutaneous administration is temperature- and volume-dependent, studies were performed to evaluate amifostine dissolution using three different volumes of the two diluents at four temperatures.

**Methods:** Amifostine 500 mg was reconstituted in 2.0, 2.5, or 2.9 mL NaCl or SWI at 15, 20, 25, and 30°C with gentle rotation in controlled water bath. Dissolution times were determined visually. Reconstituted vials were subsequently held in a water bath at 22°C for 5 hr or 4°C for 8 hr. The stability of the amifostine solution was assessed by HPLC analysis of WR-1065, the primary hydrolysis product.

**Results:** The final volume after reconstitution of amifostine 500 mg in 2.5 mL NaCl was 2.88 ± 0.04 mL, and in 2.9 mL NaCl the final volume was 3.34 ± 0.05 mL. Mean levels of WR-1065 in 2.9 mL NaCl were 0.6% ± 0.1% after 5 hr at 22°C and 0.4% ± 0.1% after 8 hr at 4°C, well below the lot-release specification of 1.3%. Dissolution times are summarized in Table 1.

**Conclusions:** Dissolution of amifostine for subcutaneous injection is volume- and temperature-dependent. Reconstitution of lyophilized amifostine powder (500 mg) with 2.9 mL NaCl or SWI (final volume, 3.3-3.4 mL) at 20-25° C, (68-77° F) results in complete dissolution within minutes. Reconstitution in smaller volumes such as

MEAN DISSOLUTION TIMES (MIN)			
°C (°F)	Diluent Volume, mL	NaCl	SWI
15 (59)	2.0	> 20	> 20
	2.5	> 20	> 20
	2.9	5:33	> 20
20 (68)	2.0	> 20	> 20
	2.5	3:36	4:19
	2.9	1:45	2:06
25 (77)	2.0	4:37	8:43
	2.5	2:03	2:24
	2.9	1:22	1:53
30 (86)	2.0	2:20	2:08
	2.5	3:08	1:39
	2.9	2:20	1:30

2.0 mL or 2.5 mL is feasible, but requires more time, and/or warmer temperature. ●

## Ongoing Prospective Multicenter Safety Study of Subcutaneous Cytoprotectant Amifostine For Head and Neck Carcinoma [5553]

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**Background:** Amifostine (Ethyol) is a radioprotectant that protects mucosal tissue from chemotherapy and radiation-induced damage. Intravenous administration is the approved route, but subcutaneous (SC) administration may offer greater ease of administration and reduced toxicity.

**Methods:** Prospective, open-label, multicenter, safety study to determine treatment-related toxicities and safety of SC administration of amifostine in preventing radiation-induced toxicities. This report focuses on patients (pts) diagnosed with head and neck carcinoma.

**Results:** One hundred sixty-six pts (121 men, 45 women, median age 61 y) received amifostine 500 mg SC before radiation therapy. Mean cumulative amifostine dose was 10,694 mg (range less than 5,000 to

INCIDENCE AND SEVERITY OF FIVE TARGETED ADVERSE EVENTS						
Targeted Adverse Event	N=166	Grade 1	Grade 2	Grade 3	Grade 4	Missing
Local Injection Site Reactions	40	29	10	1	-	-
Radiation Dermatitis	57	18	33	6	-	-
Skin Rash	26	10	13	3	-	-
Hypotension	33	21	6	5	-	1
Nausea/Vomiting	101	40	44	16	1	-

>20,000 mg); median daily dose was 500 mg and mean number of doses was 22. The most frequently reported adverse events (AEs) were nausea/vomiting (61%), radiation dermatitis (34%), local reaction (24%), hypotension (20%), and skin rash (<20%). For the majority of reports of local reaction (n=29), radiation dermatitis (n=55), and nausea/vomiting (n=54), no action was required and pts continued with study medication. Sixty-one (24%) of all

targeted AEs resulted in permanent discontinuation of amifostine owing to: local injection site reaction (n=6), radiation dermatitis (n=1), skin rash (n=16), hypotension (n=8), and nausea/vomiting (n=30). The majority (87%) of targeted AEs were grade ≤ 2, and 61% of reported serious AEs were either not related or remotely related to amifostine. The majority (96%) of pts did not require a change in amifostine

*Continued on Page 31*