



# Amifostine as a Radioprotectant

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**Drug name:** Amifostine is manufactured as Ethiol® (MedImmune Oncology, Inc., Gaithersburg, MD).

**Classification:** Cytoprotector

**Indications:** Amifostine is used as a radioprotectant in patients undergoing post-operative radiation therapy for head and neck cancer, where the radiation port includes a substantial portion of the parotid glands to reduce or prevent acute or late xerostomia. Amifostine also is used in conjunction with chemotherapy to decrease the incidence or severity of neurotoxicity, nephrotoxicity, and hematologic toxicity. Amifostine is used to minimize treatment-related sequelae without reducing the antitumor efficacy of chemotherapy or radiation therapy. Clinical trials continue to investigate its use in treating other diseases, such as lung cancer. Additional clinical trials are examining various dosing schema and alternate routes of delivery other than IV or IV bolus or “push” (IVP).

**Action:** Amifostine is taken up into the normal tissues and converted into the free thiol WR-1065. Higher levels of alkaline phosphatase and a neutral pH found in normal cells assist with the conversion process of amifostine into WR-1065.

**Metabolism:** Amifostine is dephosphorylated by membrane-bound alkaline phosphatase to its active metabolite, WR-1065.

**Excretion:** 90% of the amifostine dose is cleared from the plasma within six minutes, and the amount of prodrug that is bioconverted to the free thiol in systemic circulation is small. Amifostine and WR-1065 both are excreted by the kidneys.

**Half-life:** Amifostine is cleared from the plasma, with a distribution half-life of less than one minute and an elimination half-life of approximately eight minutes. Less than 10% of amifostine remains in the plasma six minutes after drug administration.

**Effect on blood count:** When used as a radioprotector, amifostine has no effect on blood cell counts.

**Adverse reactions:** Common side effects of amifostine include transient hypotension, nausea and vomiting (N&V), and allergic reactions. Hypotension occurs in approximately 15% of patients and can be minimized by having patients either hydrate at home orally or by giving them IV fluids prior to or during amifostine administration. Medications for hypertension may need to be held or stopped prior to amifostine administration and may be able to be resumed after administration, provided that the patient is normotensive.

N&V occurs in approximately 53% of patients. Oral or IV antiemetics are used to manage this side effect. Typically, patients receive an oral antiemetic, such as a phenothiazine or a serotonin 5-HT<sub>3</sub> receptor antagonist, and are converted to an IV antiemetic if N&V is severe or persists. Patients can take an oral antiemetic at home prior to treatment to minimize the amount of time spent in the radiation department.

Allergic reactions occur in approximately 5% of all patients. The reaction may be localized or generalized and is characterized by skin rashes, urticaria, erythema multiforme, and rare reports of anaphylactoid reactions. Patients who experience an allergic reaction may require antihistamine administration.

Other side effects, such as a warm flushing response, chills, fever, hiccoughs, and sneezing, may occur during or following infusion of the drug. Hypocalcemia is a rare side effect that may occur.

**Interactions:** Special consideration should be given to patients who are taking antihypertensives, diuretics, and other medications that could lower their blood pressure.

**Contraindications:** Amifostine is contraindicated in patients with a known sensitivity to aminothiols products. Patients unable to tolerate cessation or holding of antihypertensive drugs and patients who are hypotensive or dehydrated should not receive amifostine. Patients with preexisting cardiovascular or cerebrovascular conditions, such as ischemic heart disease, arrhythmias, congestive heart failure, or a history of stroke or transient ischemic attacks, should receive amifostine cautiously because side effects of N&V and hypotension have a more adverse effect on this patient population.

**Route and dosage:** For patients undergoing radiation therapy for squamous cell carcinoma of the head and neck, amifostine is given as a daily injection 15–30 minutes prior to radiotherapy every day at a dose of 200 mg/m<sup>2</sup>.

**Availability:** Amifostine is supplied as a sterile, white, lyophilized powder in a 10 ml glass, single-use vial.

**Dilution:** Amifostine should be reconstituted with 9.7 ml of 0.9% sodium chloride for injection, bringing the total volume to 10 ml. Each milliliter then will contain 50 mg of amifostine. The compatibility of amifostine

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