Amifostine as a Radioprotectant

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

**Classification:** Cytoprotector

**Indications:** Amifostine is used as a radioprotectant in patients undergoing postoperative 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 phe-nothiazine or a serotonin 5-HT3 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 aminothiol products. Patients unable to tolerate cessation or holding of antihypertensive 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/m2.

**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 will contain 50 mg of amifostine. The compatibility of amifostine

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Amifostine (Ethyol®) Patient Instruction Sheet

**Drug:** Ethylol® (trade name); amifostine (generic name)

**Action:** Amifostine is given to patients who have had surgery to the head and neck area prior to their radiation therapy. The medication is expected to reduce the xerostomia (i.e., dry mouth) that occurs as a result of receiving radiation to the salivary glands. A lack of saliva production can greatly affect your comfort and well-being, as well as your oral hygiene and teeth. A dry mouth makes it harder to eat and speak for longer periods of time and, in the long-term, causes tooth decay. Therefore, every effort is made to minimize this side effect.

**When do I receive the drug?** Amifostine is given as a radioprotectant when you are to receive radiation therapy to the head and neck area and the majority of your salivary glands are expected to be in the radiation field.

**How do I receive amifostine?** If your radiation oncologist feels that amifostine is indicated, the radiation oncology nurse will make arrangements for you to receive the medication daily before your radiation treatment. You will be asked to arrive at the radiation therapy department 30–45 minutes prior to your actual treatment appointment each day. The nurse will administer the amifostine intravenously 15–30 minutes prior to your therapy.

**Side effects:** The two most common side effects of amifostine are hypotension (drop in blood pressure) and nausea and vomiting. You will be instructed to drink at least four eight-ounce glasses of water in the one to two hours prior to coming for radiation to help you be well hydrated (i.e., have adequate fluid in your bloodstream and tissues) and prevent a severe drop in blood pressure. If you take medications to lower your blood pressure, let your doctor know the names of the drugs and doses. A drop in blood pressure after the administration of amifostine lasts for a very short time. If you are well hydrated, your blood pressure usually will go back to normal within 10–15 minutes. After you receive amifostine, the nurse will ask you to remain in a reclined position until your blood pressure returns to normal.

Your physician will prescribe anti-nausea medication for you to take prior to your arrival in the radiation department. The nurse will instruct you to take your medication one to two hours prior to coming for your injection. Advise your nurse or physician if you experience any nausea or vomiting despite taking this medication. Nausea and vomiting usually is felt shortly after the administration of the amifostine and, if it occurs, should not last much beyond one to two hours after treatment. If necessary, the strength of the anti-nausea medication can be increased or a combination of medications can be used to make you more comfortable.

**When to call your nurse or doctor:** Contact your physician or nurse if any of the following occur.

- Occasionally, allergic reactions occur with amifostine administration. Inform your physician or nurse if you experience any skin rashes, itching, fever, chills and shakiness, or light-headedness at times other than just after finishing an amifostine dose.
- You experience hiccoughs or sneezing after leaving the radiation therapy department.
- You experience any nausea and vomiting or if these symptoms persist during the day after you leave the radiation therapy department.

with solutions other than 0.9% sodium chloride has not been studied.

**Stability:** Amifostine can be stored at room temperature prior to reconstitution. Once reconstituted, it is stable up to five hours at room temperature or up to 24 hours refrigerated. Prior to administration, the syringe should be inspected for particulate matter and discoloration. The drug should not be used if cloudiness or precipitate is observed.

**Rate:** Amifostine should be administered via IV once daily over three minutes, 15–30 minutes prior to radiation therapy. Boccia, Alster, and Houskamp (2001) suggested that amifostine can be given safely as a 10-second IVP.

**Premedications:** Prior to the daily injection, the patient will want to take an oral antiemetic 90–120 minutes before the appointment at the radiation therapy center. Antiemetics may need to be changed and titrated according to the patient’s symptoms throughout the course of treatment. Prehydration also is recommended and initially may be oral and then switched to IV. Some patients may need to receive premedications in the radiation oncology clinic.

**Nursing implications:** Prior to the administration of amifostine, review the patient’s current weight and medications (prescription drugs and over-the-counter drugs and supplements). Verify that the patient has taken an antiemetic and completed the required prehydration. If the patient has been hydrated at home prior to the injection, instruct the patient to urinate prior to amifostine administration so that if hypotension occurs, the patient will not need to get up to void. Patients should be positioned in a reclining position during amifostine administration and for 10–15 minutes afterward. Patients may have a midline peripherally inserted catheter placed for the daily drug administration or a peripheral IV started each day. Blood pressure should be checked prior to injection and then again 5, 10, and 15 minutes postinjection. If significant hypotension occurs, the patient should be placed in the Trendelenburg position and IV hydration (250–500 cc) should be infused until the hypotension resolves. A flowsheet should be used to document the nursing care of these patients and to communicate any changes to others who may provide care. Questions regarding insurance coverage for the drug and manufacturer-sponsored financial assistance should be directed to MedImmune Oncology, Inc., at 877-633-4411 or www.medimmune.com.

**Patient education:** Patients who are going to receive amifostine should be instructed on the following during their initial consultation with the radiation oncologist and nurse.

- Antiemetic use
- Prehydration with either oral or IV fluids
- Need for IV access
- Timing of injection in relation to treatment time
- Common side effects, such as hypotension, N&V, and allergic reactions
- Less common side effects, such as chills, fever, warm flushing, hiccoughs, and sneezing
- When to contact a nurse or physician

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(Continued on page 180)
Sample Nursing Care Plan for Patients Receiving Amifostine (Ethyol®) in the Radiation Therapy Setting

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- Instruct the patient to take an oral antiemetic 90–120 minutes prior to the amifostine. IV antiemetics (if necessary) should be administered 30 minutes prior to amifostine.
- Conduct a baseline oral assessment prior to initiation of radiation therapy and weekly during treatment. Assess for xerostomia and alterations in oral mucosal integrity.
- Have the patient recline on an examination table or in a chair during and following amifostine administration because a drop in blood pressure should be anticipated. Amifostine causes vasodilation.
- Establish the patient’s baseline blood pressure and assess hydration status.
- Using sterile technique, reconstitute the amifostine with 9.7 ml of sterile 0.9% sodium chloride to result in a final concentration of 50 mg of amifostine per milliliter. Calculate and prepare the patient’s amifostine dose based on body surface area at a dose of 200 mg/m².
- Establish IV access and give amifostine as an IV push (e.g., three minutes or less) prior to the radiation treatment.
- The patient should remain reclined for 10–15 minutes following amifostine administration. Take the patient’s blood pressure 15 minutes after amifostine administration. If no change in blood pressure occurs, the patient can ambulate and receive radiation therapy treatment.
- If the patient is dehydrated, has a significant drop in blood pressure, or becomes symptomatic, administer fluids as ordered, usually 250–500 cc of normal saline over 15–30 minutes.
- Document amifostine administration and the patient’s response in the medical record.

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