

Prior Authorization DRUG Guidelines

Ethiol (amifostine)

Effective Date: 10.22.13

Date Developed: 9/3/13 by Albert Reeves MD

Last Approval Date: 1/26/16, 1/24/17, 1/23/18, 1/29/18,
1/22/19, 2/18/20

Amifostine is a prodrug converted by alkaline phosphatase to an active thiol which can bind to and thereby inhibit (“detoxify”) the reactive metabolites of cisplatin as well as scavenge free radicals generated by cisplatin or radiation therapy

Pre-authorization Criteria: Reduce the incidence of moderate-to-severe xerostomia in patients undergoing postoperative radiation treatment for head and neck cancer; reduce the cumulative renal toxicity associated with repeated administration of cisplatin

Off-Label use: prevention of radiation proctitis in patients with rectal cancer

Dosing: Cisplatin-induced renal toxicity, reduction: I.V.: 910 mg/m² once daily over 15 minutes 30 minutes prior to cytotoxic therapy (see product literature for more details)

Note: antiemetic medication, including dexamethasone 20 mg IV and a serotonin 5-HT₃ receptor antagonist, is recommended prior to infusion

Xerostomia from head and neck cancer, reduction:

I.V.: 200 mg/m² over 3 minutes once daily 15-30 minutes prior to cisplatin or radiation therapy, --or-

SubQ (unlabeled route): 500 mg once daily prior to radiation therapy

Note: extravasation may cause local tissue damage

Note: antiemetic medication, including dexamethasone 20 mg IV and a serotonin 5-HT₃ receptor antagonist, is recommended prior to infusion

Prevention of radiation proctitis in rectal cancer (off-label use): IV: 340 mg/m² once daily prior to radiation therapy

Prevention of radiation proctitis in rectal cancer (unlabeled use): I.V.: 340 mg/m² once daily prior to radiation therapy ;

How Supplied: Solution ethylol 500 mg ea)

Precautions: serious cutaneous reactions (erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, toxoderma, and exfoliative dermatitis); hypocalcemia; hypotension

Drug Interactions: antihypertensives (may enhance the hypotensive effect of amifostine)

References

1. Anne PR and Curran WJ Jr, "A Phase II Trial of Subcutaneous Amifostine and Radiation Therapy in Patients With Head and Neck Cancer," *Semin Radiat Oncol*, 2002, 12(1 Suppl 1):18-9.
2. Bonner HS and Shaw LM, "New Dosing Regimens for Amifostine: A Pilot Study to Compare the Relative Bioavailability of Oral and Subcutaneous Administration With Intravenous Infusion," *J Clin Pharmacol*, 2002, 42(2):166-74.
3. Brizel DM, Wasserman TH, Henke M, et al, "Phase III Randomized Trial of Amifostine as a Radioprotector in Head and Neck Cancer," *J Clin Oncol*, 2000, 18(19): 3339-45.
4. Capizzi RL and Oster W, "Chemoprotective and Radioprotective Effects of Amifostine: An Update of Clinical Trials," *Int J Hematol*, 2000, 72(4):425-35
5. Culy CR and Spencer CM, "Amifostine: An Update on Its Clinical Status as a Cytoprotectant in Patients With Cancer Receiving Chemotherapy or Radiotherapy and Its Potential Therapeutic Application in Myelodysplastic Syndrome," *Drugs*, 2001, 61(5):641-84
6. Hensley ML, Hagerty KL, Kewalramani T, et al, "American Society of Clinical Oncology 2008 Clinical Practice Guideline Update: Use of Chemotherapy and Radiotherapy Protectants," *J Clin Oncol*, 2009, 27(1): 127-45.
7. Keefe DM, Schubert MM, Elting LS, et al, "Updated Clinical Practice Guidelines for the Prevention and Treatment of Mucositis," *Cancer*, 2007, 109(5): 820-31.
8. Koukourakis MI, Kyrias G, and Kakolyris S, "Subcutaneous Administration of Amifostine During Fractionated Radiotherapy: A Randomized Phase II Study," *J Clin Oncol*, 2000, 18(11):2226-33.
9. Norales G, Maria V, de Guzman A, et al, "Amifostine-Induced Back Pain: a Case Report," *Am J Health-Syst Pharm*, 2006, 63(4): 381-2.
10. Peterson DE, Bensadiun RJ, and Roila F, "Management of Oral and Gastrointestinal Mucositis: ESMO Clinical Recommendations," *Ann Oncol*, 2008, 19(Suppl 2): 122-5
11. Samuels MA, Chico IM, Hirsch RL, et al, "Ongoing Prospective Multicenter Safety Study of the Cytoprotectant Amifostine Given Subcutaneously: Overview of Trial Design," *Semin Oncol*, 2003, 30(6 Suppl 18):94-5.
12. Spencer CM and Goa KL, "Amifostine. A Review of Its Pharmacodynamic and Pharmacokinetic Properties, and Therapeutic Potential as a Radioprotector and Cytotoxic Chemoprotector," *Drugs*, 1995, 50(6):1001-31
13. Wasserman TH and Brizel DM, "The Role of Amifostine as a Radioprotector," *Oncology (Huntingt)*, 2001, 15(10):1349-54.

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