

#### **Prior Authorization DRUG Guidelines**

# **Ethyol (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, 8/3/21, 2/1/22, 1/31/23, 2/13/24,

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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/m<sup>2</sup> once daily over 15 minutes 30 minutes prior to cytotoxic therapy (see product literature for more details)

### Xerostomia from head and neck cancer, reduction:

I.V.:  $200 \text{ mg/m}^2$  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

**Prevention of radiation proctitis in rectal cancer:** I.V.: 340 mg/m<sup>2</sup> 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, toxicoderma and exfoliative dermatitis); hypocalcemia. hypersensitivity reactions; hypotension; dosage adjustments necessary for kidney and renal impairment



**Note**: extravasation may cause local tissue damage

Note: antiemetic medication, including dexamethasone 20 mg IV and a serotonin 5-HT<sub>3</sub>

receptor antagonist, is recommended prior to infusion

Note: transient hypotension may occur

**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.
  - 14. Elad S, Cheng KKF, Lalla RV, et al; Mucositis Guidelines Leadership Group of the Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology (MASCC/ISOO).

    MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. Cancer. 2020;126(19):4423-4431



Peterson DE, Boers-Doets CB, Bensadoun RJ, et al. Management of oral and gastrointestinal mucosal injury: ESMO clinical practice guidelines for diagnosis, treatment, and follow-up. Ann Oncol. 2015;26(suppl 5):v139-v151.

#### **Revision History:**

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Revision Date	Content Revised (Yes/No)	Contributors	Review/Revision Notes
1/24/17	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
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2/18/20	No	Howard Taekman, MD; Robert Sterling, MD	Annual review
8/3/21	Yes	Howard Taekman, MD; Robert Sterling, MD	Updated precautions section and formatting changes.
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2/13/24	No	Howard Taekman, MD; Robert Sterling, MD	Annual review
2/18/25	Yes	Howard Taekman, MD; Robert Sterling, MD	Removed "Prevention of radiation proctitis in rectal cancer (off-label use): IV: 340 mg/m² once daily prior to radiation therapy." Updated Precautions section and added "Note: transient hypotension may occur"