BLEOMYCIN (Systemic)

Category

Antineoplastic.

Indications

Note: Bracketed information in the Indications section refers to uses that are not included in U.S. product labeling.

Accepted

Carcinoma, head and neck (treatment)

Carcinoma, laryngeal (treatment)

[Carcinoma, paralaryngeal (treatment)]

[Carcinoma, esophageal (treatment)] *

[Carcinoma, thyroid (treatment)] *

Carcinoma, cervical (treatment)

Carcinoma, penile (treatment)

[Carcinoma, skin (treatment)]

Carcinoma, vulvar (treatment) or

Carcinoma, testicular (treatment)¾Bleomycin is indicated for treatment of squamous cell carcinomas of the head and neck 1 (including the mouth, tongue, tonsil, nasopharynx, oropharynx, sinus, palate, lip, buccal mucosa, gingiva, epiglottis, and larynx 1 and paralarynx 17), cervix 1 , penis 1 , skin 17 , and vulva 1.

It is also indicated for treatment of testicular carcinoma (including embryonal cell carcinoma, choriocarcinoma, and teratocarcinoma) 1, 17 , esophageal 15, 18 , and thyroid carcinomas 7, 15.

Lymphomas, Hodgkin's (treatment) or

Lymphomas, non-Hodgkin's (treatment)¾Bleomycin is indicated for treatment of Hodgkin's and non-Hodgkin's lymphomas 1, 17.

[Kaposi's sarcoma, acquired immunodeficiency syndrome (AIDS)-associated (treatment)] *¾Bleomycin is indicated in the treatment of AIDS-associated Kaposi's sarcoma 18, 36, 37.

[Osteosarcoma (treatment)] *¾Bleomycin is indicated in the treatment of osteosarcoma 2.

Mechanism of action/Effect:

Bleomycin is classed as an antibiotic but is not used as an antimicrobial agent. Although bleomycin is effective against both cycling and non-cycling cells, it seems to be most effective in the G 2 phase of cell division 5.

Its exact mechanism of antineoplastic action is unknown but may involve binding to DNA, inducing lability of the DNA structure, and reduced synthesis of DNA, and, to a lesser extent, RNA and proteins 1.

Absorption:

Approximately 45% of a dose is absorbed into the systemic circulation following intrapleural or intraperitoneal administration.

Protein binding:

Very low (1%).

Biotransformation:

Unknown; probably by enzyme degradation in tissues (based on animal studies). Tissue enzyme activity varies, which may determine toxicity and antitumor effect of bleomycin; enzyme activity is high in the liver and kidneys, as well as in bone marrow and lymph nodes, but is low in the skin and lungs. It is not known if any metabolites are active. 5

Precautions to Consider

Carcinogenicity/Mutagenicity

Secondary malignancies are potential delayed effects of many antineoplastic agents, although it is not clear whether the effect is related to their mutagenic or immunosuppressive action. The effects of dose and duration of therapy are also unknown, although risk seems to increase with long-term use.

Carcinostatic antibiotics have been shown to be carcinogenic in animals, and have been associated with an increased risk of development of secondary carcinomas in humans.

Bleomycin has not been found to be mutagenic according to the Ames test. However, chromosomal aberrations were reported in bone marrow cells and spermatogonia of mice given very high doses.

Pregnancy/Reproduction

Fertility¾Gonadal suppression, resulting in amenorrhea or azoospermia, may occur in patients taking antineoplastic therapy, especially with the alkylating agents. In general, these effects appear to be related to dose and length of therapy and may be irreversible. Prediction of the degree of testicular or

ovarian function impairment is complicated by the common use of combinations of several antineoplastics, which makes it difficult to assess the effects of individual agents.

Pregnancy¾First trimester: It is usually recommended that use of antineoplastics, especially combination chemotherapy, be avoided whenever possible, especially during the first trimester. Although information is limited because of the relatively few instances of antineoplastic administration during pregnancy, the mutagenic, teratogenic, and carcinogenic potential of these medications must be considered.

Other hazards to the fetus include adverse reactions seen in adults.

In general, use of a contraceptive is recommended during cytotoxic drug therapy.

Bleomycin has been found to be teratogenic in mice given intraperitoneal doses of 0.6 to 5 Units per kg of body weight on days 7 to 12 of gestation; increased fetal resorptions occurred at doses of 3 and 5 Units per kg of body weight.

Breast-feeding

Although very little information is available regarding distribution of antineoplastic agents into breast milk, breast-feeding is not recommended while bleomycin is being administered because of the risks to the infant (adverse effects, mutagenicity, carcinogenicity).

Pediatrics

Appropriate studies on the relationship of age to the effects of bleomycin have not been performed in the pediatric population. However, no pediatrics-specific problems have been documented to date.

Geriatrics

Although appropriate studies on the relationship of age to the effects of bleomycin have not been performed in the geriatric population, there may be an increased risk of pulmonary toxicity in the elderly (over 70 years of age) 1.

In addition, elderly patients are more likely to have age-related renal function impairment, which may require reduction of dosage in patients receiving bleomycin.

Dental

Bleomycin may cause mild stomatitis.

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):

>> Anesthetics, general

(use in patients previously treated with bleomycin may result in rapid pulmonary deterioration because bleomycin causes sensitization of lung tissue to oxygen; even with concentrations of inspired oxygen considered to be safe, pulmonary fibrosis may develop postoperatively) 1

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