

TABLE 103e-4 CYTOTOXIC CHEMOTHERAPY AGENTS (CONTINUED)

Drug	Toxicity	Interactions, Issues
Etoposide (VP16-213)	Marrow (WBCs > platelet) Alopecia Hypotension Hypersensitivity (rapid IV) Nausea Mucositis (high dose)	Hepatic metabolism—renal 30% Reduce doses with renal failure Schedule-dependent (5-day schedule better than 1-day) Late leukemogenic Accentuate antimetabolite action
Topotecan	Marrow Mucositis Nausea Mild alopecia	Reduce dose with renal failure No liver toxicity
Irinotecan	Diarrhea: "early onset" with cramping, flushing, vomiting; "late onset" after several doses Marrow Alopecia Nausea Vomiting Pulmonary	Prodrug requires enzymatic clearance to active drug "SN 38" Early diarrhea likely due to biliary excretion Late diarrhea, use "high-dose" loperamide (2 mg q2–4 h)
Doxorubicin and daunorubicin	Marrow Mucositis Alopecia Cardiovascular acute/chronic Vesicant	Heparin aggregate; coadministration increases clearance Acetaminophen, BCNU increase liver toxicity Radiation recall
Idarubicin	Marrow Cardiac (less than doxorubicin)	None established
Epirubicin	Marrow Cardiac	None established
Mitoxantrone	Marrow Cardiac (less than doxorubicin) Vesicant (mild) Blue urine, sclerae, nails	Interacts with heparin Less alopecia, nausea than doxorubicin Radiation recall Less alopecia, nausea than doxorubicin
Indirectly DNA-Interacting Agents		
Antimetabolites		
Deoxycoformycin	Nausea Immunosuppression Neurologic Renal	Excretes in urine Reduce dose for renal failure Inhibits adenosine deaminase Reduce dose for renal failure
6-Mercaptopurine (6-MP)	Marrow Liver Nausea	Variable bioavailability Metabolize by xanthine oxidase Decrease dose with allopurinol Increased toxicity with thiopurine methyltransferase deficiency
6-Thioguanine	Marrow Liver Nausea	Variable bioavailability Increased toxicity with thiopurine methyltransferase deficiency
Azathioprine	Marrow Nausea Liver	Metabolizes to 6-MP; therefore, reduce dose with allopurinol Increase toxicity with thiopurine methyltransferase deficiency
2-Chlorodeoxyadenosine	Marrow Renal Fever	Notable use in hairy cell leukemia
Hydroxyurea	Marrow Nausea Mucositis Skin changes Rare renal, liver, lung, CNS	Decrease dose with renal failure Augments antimetabolite effect

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