

**TABLE 103e-4 CYTOTOXIC CHEMOTHERAPY AGENTS (CONTINUED)**

| Drug                      | Toxicity                                                                                                                                                                               | Interactions, Issues                                                                                                                                                                                           |
|---------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Methotrexate              | Marrow<br>Liver/lung<br>Renal tubular<br>Mucositis                                                                                                                                     | Toxicity lessened by “rescue” with leucovorin<br>Excreted in urine<br>Decrease dose in renal failure; NSAIDs increase renal toxicity                                                                           |
| 5-Fluorouracil (5FU)      | Marrow<br>Mucositis<br>Neurologic<br>Skin changes                                                                                                                                      | Toxicity enhanced by leucovorin by increasing “ternary complex” with thymidylate synthase; dihydropyrimidine dehydrogenase deficiency increases toxicity; metabolism in tissue                                 |
| Capecitabine              | Diarrhea<br>Hand-foot syndrome                                                                                                                                                         | Prodrug of 5FU due to intratumoral metabolism                                                                                                                                                                  |
| Cytosine arabinoside      | Marrow<br>Mucositis<br>Neurologic (high dose)<br>Conjunctivitis (high dose)<br>Noncardiogenic pulmonary edema                                                                          | Enhances activity of alkylating agents<br>Metabolizes in tissues by deamination but renal excretion prominent at doses >500 mg; therefore, dose reduce in “high-dose” regimens in patients with decreased CrCl |
| Azacitidine               | Marrow<br>Nausea<br>Liver<br>Neurologic<br>Myalgia                                                                                                                                     | Use limited to leukemia<br>Altered methylation of DNA alters gene expression                                                                                                                                   |
| Gemcitabine               | Marrow<br>Nausea<br>Hepatic<br>Fever/“flu syndrome”                                                                                                                                    |                                                                                                                                                                                                                |
| Fludarabine phosphate     | Marrow<br>Neurologic<br>Lung                                                                                                                                                           | Dose reduction with renal failure<br>Metabolized to F-ara converted to F-ara ATP in cells by deoxycytidine kinase                                                                                              |
| Clofarabine               | Myelosuppression<br>Mucositis<br>Rare cardiac/inflammatory                                                                                                                             |                                                                                                                                                                                                                |
| Nelarabine                | Myelosuppression<br>Neurologic                                                                                                                                                         | T cell ALL; T cell lymphoblastic lymphoma                                                                                                                                                                      |
| Asparaginase              | Protein synthesis; indirect inhibition of DNA synthesis by decreased histone synthesis<br>Clotting factors<br>Glucose<br>Albumin<br>Hypersensitivity<br>CNS<br>Pancreatitis<br>Hepatic | Blocks methotrexate action                                                                                                                                                                                     |
| Pemetrexed                | Anemia<br>Neutropenia<br>Thrombocytopenia                                                                                                                                              | Supplement folate/B <sub>12</sub><br>Caution in renal failure                                                                                                                                                  |
| Pralatrexate              | Myelosuppression<br>Mucositis                                                                                                                                                          | Active in peripheral T cell lymphoma                                                                                                                                                                           |
| <b>Antimitotic Agents</b> |                                                                                                                                                                                        |                                                                                                                                                                                                                |
| Vincristine               | Vesicant<br>Marrow<br>Neurologic<br>GI: ileus/constipation; bladder hypotoxicity; SIADH<br>Cardiovascular                                                                              | Hepatic clearance<br>Dose reduction for bilirubin >1.5 mg/dL<br>Prophylactic bowel regimen                                                                                                                     |

(Continued)