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

Drug	Toxicity	Interactions, Issues
Vinblastine	Vesicant	Hepatic clearance
	Marrow	Dose reduction as with vincristine
	Neurologic (less common but similar spectrum to other vincas)	
	Hypertension	
	Raynaud's	
Vinorelbine	Vesicant	Hepatic clearance
	Marrow	
	Allergic/bronchospasm (immediate)	
	Dyspnea/cough (subacute)	
	Neurologic (less prominent but similar spectrum to other vincas)	
Paclitaxel	Hypersensitivity	Premedicate with steroids, H_1 and H_2 blockers
	Marrow	
	Mucositis	Hepatic clearance
	Alopecia	Dose reduction as with vincas
	Sensory neuropathy	
	CV conduction disturbance	
	Nausea—infrequent	
Docetaxel	Hypersensitivity	Premedicate with steroids, H_1 and H_2 blockers
	Fluid retention syndrome	
	Marrow	
	Dermatologic	
	Sensory neuropathy	
	Nausea infrequent	
	Some stomatitis	
Estramustine phosphate	Nausea	
	Vomiting	
	Diarrhea	
	CHF	
	Thrombosis	
	Gynecomastia	
Nab-paclitaxel (protein bound)	Neuropathy	Caution in hepatic insufficiency
	Anemia	
	Neutropenia	
	Thrombocytopenia	
Ixabepilone	Myelosuppression	
	Neuropathy	

[a]Common allkylator: alopecia, pulmonary, infertility, plus teratogenesis.

Abbreviations: ALL, acute lymphocytic leukemia; AUC, area under the curve; CHF, congestive heart failure; CNS, central nervous system; CrCl, creatinine clearance; CV, cardiovascular; GI, gastrointestinal; HBP, high blood pressure; MAOI, monoamine oxidase inhibitor; NSAID, nonsteroidal anti-inflammatory drug; SIADH, syndrome of inappropriate antidiuretic hormone secretion.

myelosuppression, it causes hypnotic and other CNS effects, including vivid nightmares. It can cause a disulfiram-like syndrome on ingestion of ethanol. Altretamine (formerly hexa-methylmelamine) and thiotepa can chemically give rise to alkylating species, although the nature of the DNA damage has not been well characterized in either case. Dacarbazine (DTIC) is activated in the liver to yield the highly reactive methyl diazonium cation. It causes only modest myelosuppression 21–25 days after a dose but causes prominent nausea on day 1. Temozolomide is structurally related to dacarbazine but was designed to be activated by nonenzymatic hydrolysis in tumors and is bioavailable orally.

Cisplatin was discovered fortuitously by observing that bacteria present in electrolysis solutions with platinum electrodes could not divide. Only the *cis* diamine configuration is active as an antitumor agent. It is hypothesized that in the intracellular environment, a chloride is lost from each position, being replaced by a water molecule. The resulting positively charged species is an efficient bifunctional interactor with DNA, forming Pt-based cross-links. Cisplatin requires administration with adequate hydration, including forced diuresis with mannitol to prevent kidney damage; even with the use of hydration, gradual decrease in kidney function is common, along with noteworthy anemia. Hypomagnesemia frequently attends cisplatin use and can lead to hypocalcemia and tetany. Other common toxicities include neurotoxocity with stocking-and-glove sensorimotor neuropathy. Hearing loss occurs in 50% of patients treated with conventional doses. Cisplatin is intensely emetogenic, requiring prophylactic antiemetics. Myelosuppression is less evident than with other alkylating agents. Chronic vascular toxicity (Raynaud's phenomenon, coronary artery disease) is a more unusual toxicity. Carboplatin displays less nephro-, oto-, and neurotoxicity. However, myelosuppression is more frequent, and because the drug is exclusively cleared through the kidney, adjustment of dose for creatinine clearance must be accomplished through use of various dosing nomograms. Oxaliplatin is a platinum analogue with noteworthy activity in colon cancers refractory to other treatments. It is prominently neurotoxic.