

of intracerebral hemorrhage. It is unclear to what degree A10 contributed to hypernatremia in these patients. A10 was administered together with AS2-1, which also may contribute to hypernatremia. Serious hypernatremia was possibly related to brain tumor in 8 patients and liver disease in 2 patients. A high percentage of hypernatremia in patients can also be explained by the high sodium intake with A10 and AS2-1, because both ingredients are injected as sodium salts. Additional pharmacokinetic studies in patients receiving high dosages of A10 failed to reveal significant changes in levels of plasma electrolytes. It is recommended that patients receiving A10 have frequent monitoring of electrolytes, as described in "Administration and Dosage."

Antineoplastons A10 and AS2-1 are contraindicated in patients who have previously shown allergy to them.

Caution should be exercised and the dosage reduced when administering A10 to patients with kidney and liver impairment. Antineoplastons A10 and AS2-1 should not be used in patients who have either a leukocyte count below 1000/mm<sup>3</sup> or a platelet count below 50,000/mm<sup>3</sup>. The average sodium content of A10 is 24.5 mg/mL. Because of the sodium content of A10, it is recommended that patients with hypertension and those with a history of congestive heart failure, cardiovascular disease, or renal disease that medically contraindicate administration of high doses of sodium not be treated with A10.

### *Drug or Other Interactions*

Medications considered necessary for the patient's welfare may be given at the discretion of the treating physician. Drug interactions are not known.

### *Adverse Reactions*

Almost all patients experience increased diuresis and slight thirst. The treatment is usually free from adverse reactions or associated only with mild side effects. Moderate side effects (Grade 2 by NCI criteria) included the following: fluid retention in 0.2% of patients; hypernatremia (1.6%); hypochloremia (1.6%); hyperchloremia (0.4%); hypocalcemia (0.2%); hypokalemia (2.5%); hypomagnesemia (0.7%); nausea and vomiting (0.6%); elevation of SGPT (0.1%); leucopenia (0.1%); allergic skin rash (0.7%); fever (2.9%); chills (0.1%); headaches (0.1%); tinnitus and decreased hearing (0.7%); and decreased and blurred vision (0.2%).

Serious adverse reactions (Grade 3 and 4 by NCI criteria) were observed only in a small number of cases and included the following: hypernatremia (0.8%); hypocalcemia (0.2%); hypomagnesemia (0.1%); hypokalemia (0.1%); elevation of serum bilirubin (0.1%); SGOT (0.1%) and SGPT (0.1%); and thrombocytopenia (0.1%). It is suspected that in many cases neurologic toxicity, visual toxicity, and ototoxicity resulted from brain tumors. Serious thrombocytopenia occurred in a single patient who received combination chemotherapy 6 weeks before administration of antineoplastons, which could have contributed to bone marrow suppression. Generally, adverse reactions were fully reversible.