**Arsenic Trioxide**

**Therapeutic:** antineoplastics

**Pharmacologic:** heavy metals

**Pregnancy Category D**

**Indications**

Induction of remission and consolidation in patients with acute promyelocytic leukemia (APL) who do not respond to or tolerate retinoid and anthracycline chemotherapy and whose disease is associated with the presence of the t(15; 17) translocation or PML-RAR-alpha gene expression.

**Action**

Alters DNA and fusion proteins in leukemic cells. **Therapeutic Effects:** Improved hematologic parameters in patients with APL.

**Pharmacokinetics**

**Absorption:** IV administration results in complete bioavailability.

**Distribution:** Arsenic is stored in liver, kidney, heart, lung, hair and nails.

**Metabolism and Excretion:** Converted from pentavalent arsenic to trivalent arsenic by arsenate reductase and further converted by methyltransferases in the liver. Methylated arsenic is excreted in urine.

**Half-life:** Unknown.

**TIME/ACTION PROFILE (effect on hematologic parameters)**

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<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
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<tr>
<td>IV</td>
<td>unknown</td>
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**Contraindications/Precautions**

**Contraindicated in:** Hypersensitivity to arsenic; OB: Can cause fetal injury; Lac: Excreted in breast milk.

**Use Cautiously in:** Severe renal impairment (dose may be needed if CrCl < 30 mL/min); Hepatic impairment; Concurrent use of other drugs that cause QT interval prolongation.

**Exercise Extreme Caution in:** Pre-existing electrolyte abnormalities (correct prior to administration); concurrent use of drugs known to prolong QT interval; concurrent use of potentiation agents or amphetamines; Pedi: Children < 5 yr (safety not established).

**Adverse Reactions/Side Effects**

**CNS:** Fatigue, headache, insomnia, weakness.

**Resp:** Hypoxia, dyspnea, pleural effusion.

**CV:** Torsades de pointes, complete AV block, atrial arrhythmias, QT interval prolongation.

**GI:** Abdominal pain, constipation, liver enzymes.

**GU:** Renal failure.

**Derm:** Dermatitis.

**Endo:** Hyperglycemia, hypoglycemia.

**F and E:** Acidosis, hypocalcemia, hyperkalemia, hypokalemia, hypomagnesemia.

**Hemat:** Neutropenia, APL differentiation syndrome, disseminated intravascular coagulation, thrombocytopenia, hyperleukocytosis, anemia, leukocytosis, MR back pain, arthralgia, bone pain, neck pain, limb pain, myalgia.

**Misc:** Allergic reactions, fever, infection/sepsis.

**Interactions**

**Drug-Drug:** Use cautiously with other agents known to cause QT prolongation including some antiarrhythmics or thioridazine. Concurrent use of amphotericin B, potassium- or magnesium-wasting diuretics (risk of serious arrhythmias).

**Route/Dosage**

**IV (Adults and Children > 5 yr):**

- **Induction—** 0.15 mg/kg/day until bone marrow remission (not to exceed 60 doses);
- **Consolidation—** starting 3–6 wk after completion of induction; 0.15 mg/kg/day for 25 doses over a period of 5 wk.

**NURSING IMPLICATIONS**

**Assessment**

- **Bone Marrow Aspiration (Bone Marrow Aspiration):** Hydroxyurea — 15 mg/kg/day until bone marrow remission (not to exceed 60 doses). Consolidation — starting 3–6 wk after completion of induction; 0.15 mg/kg/day for 25 doses over a period of 5 wk.

**Exercise Extreme Caution in:** Pre-existing electrolyte abnormalities (correct prior to administration); concurrent use of drugs known to prolong QT interval; concurrent use of potentiation agents or amphetamines; Pedi: Children < 5 yr (safety not established).

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tion phase. May cause QT interval prolongation and may lead to a torsade de pointes-type arrhythmia, which may be fatal, and complete atrioventricular block. Risk of arrhythmia is increased with increased QT prolongation, concurrent administration of QT prolonging drugs, history of torsade de pointes, pre-existing QT interval prolongation, HF, administration of potassium-wasting diuretics, or other conditions resulting in hypokalemia or hypomagnesemia. Drugs known to cause prolonged QT interval should be discontinued if possible. For QTc >500 msec, corrective measures should be completed and QTc reassessed with serial ECGs prior to initiation of therapy. If QTc increases to >500 msec, reassess and take immediate corrective action and consider risk/benefit ratio of therapy. If syncope, rapid or irregular heartbeat develops, patient should be hospitalized for monitoring, serum electrolytes assessed, and therapy should be discontinued until the QTc interval is <500 msec; electrolyte abnormalities are corrected, and syncope and/or irregular heartbeat cease.

- Monitor vital signs periodically throughout therapy. May cause hypotension or hypertension.

- Lab Test Considerations: Monitor electrolyte, hematologic, and coagulation profiles at least twice weekly and more frequently for clinically unstable patients during induction phase and at least weekly during consolidation phase. May cause hypokalemia, hypophosphatemia, hypomagnesemia, hyperglycemia, hypocalcemia, and anemia. Potassium levels should be kept above 3.5 mEq/L and magnesium concentrations should be kept above 1.8 mg/dL during therapy.

- Toxicity and Overdose: Symptoms of acute arsenic toxicity include convulsions, muscle weakness, and confusion. If these symptoms occur, discontinue therapy immediately and consider chelation therapy. Protocol for arsenic intoxication includes dimercaprol 3 mg/kg IM every 4 hr until immediate life-threatening toxicity has subsided. Then penicillamine 250 mg PO up to 4 times/day (100 mg/day) may be given.

- Potential Nursing Diagnoses

- Risk for injury (Side Effects)