

Tretinoin

Class: Antineoplastic Agent, Retinoic Acid Derivative

Indications:

Induction of remission in patients with acute promyelocytic leukemia (APL), French American British (FAB) classification M3 (including the M3 variant) characterized by t(15;17) translocation and/or PML/RAR $\hat{\pm}$ gene presence.

Unlabeled Use: Post consolidation and maintenance therapy in APL; combination therapy (with arsenic trioxide) for remission induction in APL

Available dosage form in the hospital: 10MG CAPS

Dosage: Details concerning dosing in combination regimens should also be consulted. **Note:** Induction treatment of APL with tretinoin should be initiated early; discontinue if pending cytogenetic analysis does not confirm t(15;17) translocation or the presence of the PML/RAR $\hat{\pm}$ fusion protein.

-Acute promyelocytic leukemia (APL): Oral:

- *Remission induction (in combination with an anthracycline \pm cytarabine; unlabeled use):* 45 mg/m²/day in 2 equally divided doses until complete remission or 90 days or until complete hematologic remission
- *Remission induction (in combination with arsenic trioxide; unlabeled use):* 45 mg/m²/day in 2 equally divided doses until <5% blasts in marrow and no abnormal promyelocytes or up to 85 days
- *Consolidation therapy (unlabeled use):* 45 mg/m²/day in 2 equally divided doses for 15 days each month for 3 months (in combination with chemotherapy **or** 45 mg/m²/day for 14 days every 4 weeks for 7 cycles (in combination with arsenic trioxide)
- *Maintenance therapy, intermediate- and high-risk patients (unlabeled use):* 45 mg/m²/day in 2 equally divided doses for 15 days every 3 months for 2 years.

Dosing: Adjustment for Toxicity

- APL differentiation syndrome: Initiate dexamethasone 10 mg I.V. every 12 hours for 3-5 days; consider interrupting tretinoin until resolution of hypoxia
- Liver function tests >5 times the upper limit of normal: Consider temporarily withholding treatment
- For combination regimens, look for specific protocols

Common side effect:

Cardiovascular: Peripheral edema (52%), chest discomfort (32%), edema (29%), arrhythmias (23%), flushing (23%), hypotension (14%), hypertension (11%)

Central nervous system: Headache (86%), fever (83%), malaise (66%), pain (37%), dizziness (20%), anxiety (17%), depression (14%), insomnia (14%), confusion (11%)

Dermatologic: Skin/mucous membrane dryness (77%), rash (54%), pruritus (20%), alopecia (14%), skin changes (14%)

Endocrine & metabolic: Hypercholesterolemia and/or hypertriglyceridemia ($\leq 60\%$)

Gastrointestinal: Nausea/vomiting (57%), GI hemorrhage (34%), abdominal pain (31%), mucositis (26%), diarrhea (23%), weight gain (23%), anorexia (17%), constipation (17%), weight loss (17%), dyspepsia (14%), abdominal distention (11%)

Hematologic: Hemorrhage (60%), leukocytosis (40%), disseminated intravascular coagulation (DIC) (26%)

Hepatic: Liver function tests increased (50% to 60%)

Local: Phlebitis (11%)

Neuromuscular & skeletal: Bone pain (77%), paresthesia (17%), myalgia (14%)

Ocular: Ocular disorder (17%), visual disturbances (17%)

Otic: Earache/ear fullness (23%)

Renal: Renal insufficiency (11%)

Respiratory: Upper respiratory tract disorders (63%), dyspnea (60%), respiratory insufficiency (26%), pleural effusion (20%), expiratory wheezing (14%), pneumonia (14%), rales (14%)

Miscellaneous: Shivering (63%), infections (58%), retinoic acid-acute promyelocytic leukemia syndrome differentiation syndrome ($\leq 25\%$), diaphoresis (20%)

Pregnancy Risk Factor: D