procarbazine (proe-kar-bae-zeen)

Matulane, Natulan

Classification
Therapeutic: antineoplastics
Pharmacologic: alkylating agents

Pregnancy Category D

Indications

Action
Appears to inhibit DNA, RNA, and protein synthesis (cell-cycle S-phase–specific).

Therapeutic Effects:
Death of rapidly replicating cells, particularly malignant ones.

Pharmacokinetics
Absorption: Well absorbed following oral administration.
Distribution: Widely distributed; crosses the blood-brain barrier.
Metabolism and Excretion: Metabolized by the liver; 5% excreted unchanged by the kidneys; some respiratory elimination as methane and carbon dioxide.
Half-life: 1 hr.

TIME/ACTION PROFILE (effects on blood counts)

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
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</thead>
<tbody>
<tr>
<td>PO</td>
<td>14 days</td>
<td>2–8 wk</td>
<td>28 days or more (up to 6 wk)</td>
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</tbody>
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Contraindications/Precautions
Contraindicated in: Hypersensitivity; Alcoholism; Severe renal or liver impairment; Pregnancy or lactation. OB, Lactation: Pregnancy or lactation.

Use Cautiously in: Infection; Bone marrow reserve; Headache; Psychiatric illness; Liver impairment; Cardiovascular disease; OB: Women with childbearing potential should be advised to avoid pregnancy. Pedi: Very close clinical monitoring required due to potential for toxicity.

Adverse Reactions/Side Effects

Interactions
Drug-Drug: Concurrent use with sympathomimetics including methylphenidate may produce life-threatening hypertension (avoid concurrent use during and for 14 days following procarbazine). Deep coma and death may result from concurrent use of opioid analgesics; avoid meperidine. Use small incremental doses of other agents and titrate to effect. CNS depression may occur with other antimetics or radiation therapy. Seizures and hypepyrexia may occur with concurrent use of MAO inhibitors, tricyclic antidepressants. SSRI antidepressants (should not be used within 5 wk of Fluoxetine), or carbamazepine. Myelosuppression may occur with concurrent use of radiation therapy. CNS depression may occur with concurrent use of other CNS depressants, including alcohol, antihistamines, antidepressants, opioid analgesics, phenothiazines, and sedative/hypnotics. Disulfiram-like reaction may occur with alcohol.

Drug-Food: Ingestion of foods high in tyramine content may result in hypertensive crisis. Consumption of foods high in caffeine content may result in arrhythmias.

Route/Dosage
PO (Adults): 2–4 mg/kg/day as a single dose or in divided doses for 1 wk, then 4–6 mg/kg/day until response is obtained; then maintenance dose of 1–2 mg/kg/day. Dosage should be rounded off to the nearest 50 mg. PO (Children): 50 mg/m2/day for 7 days, then 100 mg/m2/day, maintenance dose of 50 mg/m2/day.

Pharmacologic ACTIONS
- ONSET:
- PEAK:
- DURATION:
- CONTRAINDICATIONS/ PRECAUTIONS:
- ADVERSE REACTIONS:
- INTERACTIONS:
- ROUTE:
- DOSAGE:
- CLINICAL EFFICACY:
- CLINICAL SAFETY:
- CLINICAL MONITORING:
- CLINICAL MANAGEMENT:
- CLINICAL REMARKS:
- CLINICAL REFERENCES:
- CLINICAL TIPS:
- CLINICAL ALERTS:
NURSING IMPLICATIONS

Assessment

- Monitor BP, pulse, and respiratory rate periodically during therapy. Report significant changes to health care professional.
- Assess nutritional status (appetite, intake and output ratios, weight, frequency and amount of emesis). Anorexia and weight loss can be decreased by feeding light, frequent meals. Nausea and vomiting can be minimized by administering an antiemetic at least 1 hr prior to receiving medication. Phenothiazine antiemetics should be avoided.
- Monitor for bone marrow depression. Assess for bleeding (bleeding gums, bruising, petechiae, guaiac stools, urine, and emesis) and avoid IM injections and taking rectal temperatures if platelet count is low. Apply pressure to venipuncture sites for 10 min. Assess for signs of infection during neutropenia. Fever may occur. Monitor for increased fatigue, diarrhoea, and orthostatic hypotension.

Concurrent ingestion of tyramine-rich foods and many medications may result in life-threatening hypertensive crisis. Signs and symptoms of hypertensive crisis include chest pain, severe headache, nausea and vomiting, photosensitivity, and enlarged pupils. Treatment includes IV phentolamine.

- Precautions should be discontinued and side effects cleared and then resumed at a lower dose if leukopenia, thrombocytopenia, hypersensitivity reaction, stomatitis (first small ulceration or persistent soreness), diarrhea, hematuria, or bleeding tendencies occur.

Lab Test Considerations:

- Monitor hemoglobin, hematocrit, WBC, differential, reticulocytes, and platelet count prior to and every 3–4 days during therapy. Notify physician if WBC \( < 4000/\text{mm}^3 \) or platelet count \( < 100,000/\text{mm}^3 \). Therapy should be discontinued and resumed at a lower dose when counts improve. The nadir of leukopenia and thrombocytopenia occurs in approximately 2–9 wk, and recovery may occur at the rate of 1000/mm\(^3\)/wk. Anemia also may occur.

- Assess hepatic and renal function prior to therapy. Monitor urinalysis, AST, ALT, alkaline phosphatase, and BUN at least weekly during therapy.

- Closely monitor serum glucose in diabetic patients. Oral hypoglycemics or insulin dosage may need to be reduced, because hypoglycemic effects are enhanced.

- Bone marrow aspiration studies may be recommended prior to initiation of therapy and at time of maximum hematologic response to ensure adequate bone marrow reserve.

Potential Nursing Diagnoses

- Risk for infection (Adverse Reactions)
- Imbalanced nutrition: less than body requirements (Adverse Reactions)

Implementation

- PO: Administer with food or fluids if GI irritation occurs. Confer with pharmacist regarding opening of capsules if patient has difficulty swallowing.

Patient/Family Teaching

- Emphasize the need to take medication as directed. Take missed doses as soon as remembered within a few hours but not if several hours have passed or if almost time for next dose. Health care professional should be consulted if vomiting occurs shortly after a dose is taken.

- Instruct patient to notify health care professional promptly if signs of infection (fever, sore throat, chills, cough) occur. Bleeding gums, bruising, petechiae, or blood in stool, urine, or emesis occurs. Caution patient to avoid crowds and persons with known infections. Instruct patient to use soft toothbrush and electric razor and to avoid falls. Patient should not receive IM injections or rectal temperatures. Caution patient to drink alcohol, caffeinated beverages, OTC decongestants, cough syrup, or cold preparations containing aspirin or NSAIDs; they may precipitate gastric bleeding.

- Advise patient to avoid alcohol, caffeinated beverages, CNS depressants, OTC drugs, and foods or beverages containing tyramine during therapy and for at least 2 wk after therapy has been discontinued, because they may precipitate a hypertensive crisis.

- Advise patient that an additional interaction of alcohol with procainamide is a disulfiram-like reaction (flushing, nausea, vomiting, headache, abdominal cramps).

- Instruct patient to inspect oral mucosa for erythema and ulceration. If ulceration occurs, advise patient to notify health care professional and to use soft toothbrush and electric razor.

- Advise patient that this medication may have teratogenic effects. Contraception should be practiced during therapy and for at least 6 mos after therapy is concluded.

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procarbazine

- Discuss the possibility of hair loss with patient. Explore methods of coping.
- Caution patient to use sunscreen and protective clothing to prevent photosensitivity reactions.
- Instruct patient not to receive any vaccinations without advice of health care professional.
- Advise patient to notify health care professional of medication regimen prior to treatment or surgery. This therapy usually should be withdrawn at least 2 wk prior to surgery.
- Instruct patient to consult health care professional if muscle or joint pain, nausea, vomiting, diarrhea, headache, drowsiness, confusion, weakness, numbness, or loss of appetite becomes pronounced.
- Advise patient to carry identification describing medication regimen at all times.
- Emphasize the importance of periodic lab tests to monitor for side effects.

Evaluation/Desired Outcomes

- Decrease in size and spread of malignant tissue in Hodgkin’s disease.

Why was this drug prescribed for your patient?