dacarbazine (da-kar-ba-zeen)

- High Alert

**Classification**
- Therapeutic: antineoplastics
- Pharmacologic: alkylating agents

**Pregnancy Category C**

**Indications**
- Treatment of metastatic malignant melanoma (single agent).
- Treatment of Hodgkin's disease as second-line therapy (with other agents).

**Action**
- Disrupts DNA and RNA synthesis (cell-cycle phase - nonspecific). Therapeutic Effects: Death of rapidly growing tissue cells, especially malignant ones.

**Pharmacokinetics**
- **Absorption:** IV administration results in complete bioavailability.
- **Distribution:** Large volume of distribution; probably concentrates in liver; some CNS penetration.
- **Metabolism and Excretion:** 50% metabolized by the liver, 50% excreted unchanged by the kidneys.
- **Half-life:** 5 hours (q 24 hours in renal and hepatic dysfunction).

**TIME/ACTION PROFILE (effects on blood counts)**

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV (WBCs)</td>
<td>16–20 days</td>
<td>21–25 days</td>
<td>3–5 days</td>
</tr>
<tr>
<td>IV (platelets)</td>
<td>unknown</td>
<td>16 days</td>
<td>3–5 days</td>
</tr>
</tbody>
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**Contraindications/Precautions**
- **Contraindicated in:** Hypersensitivity.
- **Use Cautiously in:** Active infections; Bone marrow depression; Pedi: Children (safety not established); Renal dysfunction; Hepatic dysfunction.

**Adverse Reactions/Side Effects**
- **GI:** HEPATIC NECROSIS, anorexia, nausea, vomiting, diarrhea, hepatic vein thrombosis.
- **Derm:** alopecia, rash, erythema multiforme, Stevens-Johnson syndrome.
- **Hemat:** anemia, thrombocytopenia, neutropenia. Local: pain at IV site, phlebitis at IV site, local skin irritation.
- **Endo:** gonadal suppression.
- **Local:** pain at IV site, phlebitis at IV site, local skin irritation.
- **MS:** myalgia.
- **Neuro:** facial paresthesia.
- **Misc:** ANAPHYLAXIS, fever, flu-like syndrome, malaise.

**Interactions**
- **Drug-Drug:** Additive bone marrow depression with other antineoplastics. Carbamazepine, phenobarbital, and rifampin may q metabolism and decrease effectiveness. Blood levels may be q with amiodarone, ciprofloxacin, fluoroquinolones, ketoconazole, ofloxacin, isoniazid, or miconazole. May q anti- body response to live-virus vaccines and q risk of adverse reactions.

**Route/Dosage**
- Other regimens are used.
  - **IV (Adults):** Malignant melanoma—2–4.5 mg/kg/day for 10 days administered every 4 wk or 250 mg/m²/day for 5 days administered every 3 wk. Hodgkin's disease—150 mg/m²/day for 5 days (in combination with other agents) administered every 4 wk or 375 mg/m² (in combination with other agents) administered every 15 days.

**NURSING IMPLICATIONS**
- **Assessment**
  - Monitor vital signs prior to and frequently during therapy.
  - Monitor for bone marrow depression. Assess for bleeding (bleeding gums, bruising, petechiae, black stools, urine, and emesis) and avoid infections.
  - Monitor temperature; if temperature is elevated, assess for infection during neutropenia. Anorexia occurs. Monitor for increased fatigue, depression, and orthostatic hypotension.
  - Monitor IV site closely. Dacarbazine is an irritant. Instruct patient to notify health care professional immediately if discomfort at IV site occurs. Discontinue IV immediately if infiltration occurs. Applications of hot packs may relieve pain, burning sensation, and irritation at injection site.
  - Monitor intake and output, appetite, and nutritional intake. Assess for nausea and vomiting, which may be severe and last 1–2 hr. Administration of an antiemetic prior to and periodically during therapy, restricting oral intake for 4–6 hr prior to administration, and administering diet as tolerated may help maintain fluid and electrolyte balance and nutritional status. Nausea usually decreases on subsequent doses.

**High Alert**
- **CNS depression, respiratory depression, hypotension, and cardiovascular collapse may occur.**
Lab Test Considerations: Monitor CBC and differential prior to and periodically throughout therapy. The nadir of thrombocytopenia occurs in 10 days. The nadir of leukopenia occurs in 1–4 wk. Recovery begins in 5 days. Withhold dose and notify physician if platelet count is <100,000/mm³ or leukocyte count is <4000/mm³.

Monitor for increased AST, ALT, BUN, and serum creatinine. May cause hepatic necrosis.

Potential Nursing Diagnoses
- Risk for infection (Side Effects)
- Risk for injury (Side Effects)

Implementation
- High Alert: Fatalities have occurred with chemotherapeutic agents. Before administering, clarify all ambiguous orders; double-check single, daily, and course-of-therapy dose limits; have second practitioner independently double-check original order, calculations, and infusion pump settings.

IV Administration
- pH: 3.0–4.0.
- Prepare solution in a biosafe cabinet. Wear gloves, gown, and mask while handling medication. Discard equipment in designated containers.
- Reconstitute each 200-mg vial with 19.7 mL of sterile water for injection. Solution is colorless or clear yellow. Do not use solution that has turned pink.
- Concentration: 10 mg/mL. Solution is stable for 8 hr at room temperature and for 72 hr if refrigerated.

Intermittent Infusion: Diluent: Further dilute with up to 250 mL of D5W or 0.9% NaCl. Stable for 24 hr if refrigerated or 8 hr at room temperature. Rate: Administer over 30–60 min.

Y-Site Compatibility: amifostine, aztreonam, bivalirudin, caspofungin, daptomycin, dexmedetomidine, docetaxel, doxorubicin liposome, ertapenem, etoposide phosphate, fenoldopam, filgrastim, fludarabine, granisetron, hetastarch, levofloxacin, mechlorethamine, melphalan, nesiritide, octreotide, ondansetron, oxaliplatin, paclitaxel, palonosetron, quinupristin/dalfopristin, sargramostim, teniposide, thiotepa, tigecycline, tirofiban, vinorelbine, voriconazole.

Y-Site Incompatibility: allopurinol, amphotericin B liposome, cefepime, pantoprazole, piperacillin/tazobactam.

Patient/Family Teaching
- Instruct patient to notify health care professional if fever, chills, sore throat, signs of infection; bleeding gums; bruising; petechiae; abdominal pain; yellowing of eyes or blood in urine, stool, or emesis occurs. Caution patient to avoid crowds and persons with known infections. Instruct patient to use soft toothbrush and electric razor. Patients should be cautioned not to drink alcoholic beverages or take products containing aspirin or NSAIDs, may increase GI irritation.
- May cause photosensitivity. Instruct patient to avoid sunlight or wear protective clothing and use sunscreen for 2 days after therapy.
- Instruct patient to inform health care professional if skin Rash, photosensitivity occurs. Symptoms include fever, erythema, and generalized malaise. May occur after several courses of therapy. Usually occurs 5 wk after administration. May persist for 1–3 wk. Acetaminophen may be used for relief of symptoms.
- Discuss with patient the possibility of hair loss. Explore coping strategies.
- Instruct patient to use nonhormonal method of contraception.
- Advise patient not to receive any vaccinations without advice of health care professional.

Evaluation/Desired Outcomes
- Decrease in size and spread of malignant melanoma or Hodgkin’s lymphoma.

Path/Family Teaching
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Why was this drug prescribed for your patient?