AVENACY

Melphalan

Hydrochloride for Injection

50 mg

NDC 83634-202-61

50 mg per vial

DESCRIPTION	Single-Dose Vial
CONCENTRATION	50 mg per vial
CLOSURE	20 mm
UNIT OF SALE	1 Kit
BAR CODED	Yes
STORAGE	Room Temp.

10 mL

10 mL Diluent

DESCRIPTION	Single-Dose Vial
FILL VOLUME	10 mL
CLOSURE	20 mm
BAR CODED	Yes
STORAGE	Room Temp.

• AP RATED • PRESERVATIVE-FREE • NOT MADE WITH NATURAL RUBBER LATEX •

PLEASE SEE IMPORTANT SAFETY INFORMATION ATTACHED, INCLUDING BOXED WARNING.

VISIT WWW.AVENACY.COM/PRODUCTS/MELPHALAN-HYDROCHLORIDE-FOR-INJECTION FOR FULL PRESCRIBING INFORMATION.

ORDER THROUGH YOUR WHOLESALER:

STRENGTH	CENCORA/ABC	Cardinal	McKesson	Morris Dickson
50 mg per vial	**10286053**	**5895222**	**2906915**	**366567**

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MELPHALAN Hydrochloride for Injection

INDICATIONS AND USAGE

- Melphalan Hydrochloride for Injection is indicated for the palliative treatment of patients with multiple myeloma for whom oral therapy is not appropriate.

IMPORTANT SAFETY INFORMATION

WARNING

MELPHALAN SHOULD BE ADMINISTERED UNDER THE SUPERVISION OF A QUALIFIED PHYSICIAN EXPERIENCED IN THE USE OF CANCER CHEMOTHERAPEUTIC AGENTS. SEVERE BONE MARROW SUPPRESSION WITH RESULTING INFECTION OR BLEEDING MAY OCCUR. CONTROLLED TRIALS COMPARING INTRAVENOUS (IV) TO ORAL MELPHALAN HAVE SHOWN MORE MYELOSUPPRESSION WITH THE IV FORMULATION. HYPERSENSITIVITY REACTIONS, INCLUDING ANAPHYLAXIS, HAVE OCCURRED IN APPROXIMATELY 2% OF PATIENTS WHO RECEIVED THE IV FORMULATION. MELPHALAN IS LEUKEMOGENIC IN HUMANS. MELPHALAN PRODUCES CHROMOSOMAL ABERRATIONS IN VITRO AND IN VIVO AND, THEREFORE, SHOULD BE CONSIDERED POTENTIALLY MUTAGENIC IN HUMANS.

CONTRAINDICATIONS

- Melphalan should not be used in patients whose disease has demonstrated prior resistance to this agent. Patients who have demonstrated hypersensitivity to melphalan should not be given the drug.

WARNINGS and PRECAUTIONS

- **Extravasation:** Melphalan hydrochloride for injection may cause local tissue damage should extravasation occur, and consequently it should not be administered by direct injection into a peripheral vein. It is recommended that melphalan hydrochloride for injection be administered by injecting slowly into a fast-running IV infusion via an injection port, or via a central venous line.
- **Melphalan hydrochloride for injection should be administered in carefully adjusted dosage by or under the supervision of experienced physicians who are familiar with the drug's actions and the possible complications of its use.**
- **Bone Marrow Suppression:** Bone marrow suppression is the most significant toxicity associated with melphalan hydrochloride for injection in most patients. Hematologic tests (platelet count, hemoglobin, white blood cell count, and differential) should be performed at the start of therapy and prior to each subsequent dose. Thrombocytopenia or leukopenia are indications to withhold further therapy until the blood counts have sufficiently recovered. Dose adjustments should be considered on the basis of blood counts at the nadir and day of treatment. Use with extreme caution in patients whose bone marrow reserve may have been compromised by prior irradiation or chemotherapy or whose marrow function is recovering from previous cytotoxic therapy.
- **Hypersensitivity Reactions:** Hypersensitivity reactions including anaphylaxis have occurred in approximately 2% of patients who received the IV formulation of melphalan. These reactions usually occur after multiple courses of treatment. Treatment is symptomatic. The infusion should be terminated immediately, followed by the administration of volume expanders, pressor agents, corticosteroids, or antihistamines at the discretion of the physician. If a hypersensitivity reaction occurs, IV or oral melphalan should not be readministered since hypersensitivity reactions have also been reported with oral melphalan.
- **Secondary Malignancies:** Secondary malignancies, including acute nonlymphocytic leukemia, myeloproliferative syndrome, and carcinoma, have been reported in patients with cancer treated with alkylating agents (including melphalan). Precise quantitation of the risk of acute leukemia, myeloproliferative syndrome, or carcinoma is not possible. Published reports of leukemia in patients who have received melphalan (and other alkylating agents) suggest that the risk of leukemogenesis increases with chronicity of treatment and with cumulative dose, although this does not mean that there is a cumulative dose below which there is no risk of the induction of secondary malignancy. The potential benefits from melphalan therapy must be weighed on an individual basis against the possible risk of the induction of a second malignancy.
- **Genetic Effect:** Melphalan has been shown to cause chromatid or chromosome damage in humans.
- **Use in Specific Populations:**
  - Melphalan causes suppression of ovarian function in premenopausal women, resulting in amenorrhea in a significant number of patients. Reversible and irreversible testicular suppression have also been reported.
  - Melphalan is a pregnancy category D agent and may cause fetal harm when administered to a pregnant woman. Women of childbearing potential should be advised to avoid becoming pregnant.
  - It is not known whether this drug is excreted in human milk. IV melphalan should not be given to nursing mothers.
  - Dose reduction should be considered in patients with renal insufficiency receiving IV melphalan.
  - Administration of live vaccines to immunocompromised patients should be avoided.
- **Drug Interactions:** The development of severe renal failure has been reported in patients treated with a single dose of IV melphalan followed by standard oral doses of cyclosporine. Cisplatin may affect melphalan kinetics by inducing renal dysfunction and subsequently altering melphalan clearance. IV melphalan may also reduce the threshold for BCNU lung toxicity. When nalidixic acid and IV melphalan are given simultaneously, the incidence of severe hemorrhagic necrotic enterocolitis has been reported to increase in pediatric patients.

ADVERSE REACTIONS

- The most common side effect is bone marrow suppression leading to leukopenia, thrombocytopenia, and anemia. Blood count nadirs usually occur 2 to 3 weeks after treatment.
- Gastrointestinal disturbances such as nausea and vomiting, diarrhea, and oral ulceration occur infrequently. Hepatic disorders ranging from abnormal liver function tests to clinical manifestations such as hepatitis and jaundice have been reported. Hepatic veno-occlusive disease has been reported.

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- Acute hypersensitivity reactions can occur in patients receiving melphalan hydrochloride for injection, characterized by urticaria, pruritus, edema, skin rashes, and in some patients, tachycardia, bronchospasm, dyspnea, hypotension, and rarely, cardiac arrest. Patients may respond to antihistamine and corticosteroid therapy.
- Other reported adverse reactions include skin hypersensitivity, skin ulceration at injection site, skin necrosis rarely requiring skin grafting, maculopapular rashes, vasculitis, alopecia, hemolytic anemia, allergic reaction, pulmonary fibrosis (including fatal outcomes), and interstitial pneumonitis. Temporary significant elevation of the blood urea has been seen in the early stages of therapy in patients with renal damage. Subjective and transient sensation of warmth or tingling can occur.

OVERDOSAGE

- The principal toxic effect of overdosage with melphalan is bone marrow suppression. Hematologic parameters should be closely followed for 3 to 6 weeks. Administration of autologous bone marrow or hematopoietic growth factors may shorten the period of pancytopenia.
- General supportive measures together with appropriate blood transfusions and antibiotics should be instituted as deemed necessary.
- Melphalan is not removed from plasma to any significant degree by hemodialysis or hemoperfusion.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch. Or call 1-800-FDA-1088.

Please see full prescribing information for MELPHALAN Hydrochloride for Injection.