Melphalan

Class: Alkylating Agent (classical)

Indications :

_Palliative treatment of multiple myeloma

_nonresectable epithelial ovarian carcinoma

_Amyloidosis(unlabeled)

_Hodgkin lymphoma(unlabeled)

Available dosage form in the hospital:2 MG TAB

Trade name : Alkeran

Doses: Details regarding dosing in combination regimens should also be consulted. Adjust dose based on patient response and weekly blood counts.

-**Multiple myeloma (palliative treatment): Note:** Response is gradual; may require repeated courses to realize benefit:

-Oral: Usual dose (as described in the manufacturer's labeling):

- 6 mg once daily for 2-3 weeks initially, followed by up to 4 weeks rest, then a maintenance dose of 2 mg daily as hematologic recovery begins **or**
- 10 mg daily for 7-10 days; institute 2 mg daily maintenance dose after WBC >4000 cells/mm^3 and platelets >100,000 cells/mm^3 (~4-8 weeks); titrate maintenance dose to hematologic response **or**
- 0.15 mg/kg/day for 7 days, with a 2-6 week rest, followed by a maintenance dose of ≤0.05 mg/kg/day as hematologic recovery begins **or**
- 0.25 mg/kg/day for 4 days (or 0.2 mg/kg/day for 5 days); repeat at 4- to 6-week intervals as ANC and platelet counts return to normal

Other dosing regimens in ***combination therapy* (unlabeled doses):*

- 4 mg/m^2/day for 7 days every 4 weeks (in combination with prednisone **or** with prednisone and thalidomide) **or**
- 6 mg/m^2/day for 7 days every 4 weeks (in combination with prednisone) **or**
- 0.25 mg/kg/day for 4 days every 6 weeks (in combination with prednisone **or** with prednisone and thalidomide) **or**
- 9 mg/m^2/day for 4 days every 6 weeks (in combination with prednisone **or** with prednisone and bortezomib)

-I.V.: 16 mg/m^2 administered at 2-week intervals for 4 doses, then administer at 4-week intervals after adequate hematologic recovery.

-**Ovarian carcinoma:** Oral: 0.2 mg/kg/day for 5 days, repeat every 4-5 weeks **or**

Unlabeled dosing: 7 mg/m^2/day in 2 divided doses for 5 days, repeat every 28 days

-Amyloidosis, light chain (unlabeled use): Oral: 0.22 mg/kg/day for 4 days every 28 days (in combination with oral dexamethasone) **or** 10 mg/m^2/day for 4 days every month (in combination with oral dexamethasone) for 12-18 treatment cycles

-Hodgkin lymphoma (unlabeled use): I.V.: 30 mg/m^2 on day 6 of combination chemotherapy (mini-BEAM) regimen

-Conditioning regimen for autologous hematopoietic stem cell transplantation (unlabeled use): I.V.:

- 200 mg/m^2 alone 2 days prior to transplantation **or**
- 140 mg/m^2 2 days prior to transplantation (combined with busulfan) **or**
- 140 mg/m^2 2 days prior to transplantation (combined with total body irradiation [TBI]) **or**
- 140 mg/m^2 5 days prior to transplantation (combined with TBI)

Geriatric
Refer to adult dosing. Use caution and begin at the lower end of dosing range.

Renal Impairment:
The FDA-approved labeling contains the following adjustment recommendations (for approved dosing levels) based on route of administration:
- Oral: Moderate-to-severe renal impairment: Consider a reduced dose initially.
- I.V.: BUN ≥30 mg/dL: Reduce dose by up to 50%.

The following guidelines have been used by some clinicians:
-Aronoff, 2007 (route of administration not specified): Adults (based on a 6 mg once-daily dose):
- Cl_{cr} 10-50 mL/minute: Administer 75% of dose.
- Cl_{cr} <10 mL/minute: Administer 50% of dose.
- Hemodialysis: Administer dose after hemodialysis.
- Continuous ambulatory peritoneal dialysis (CAPD): Administer 50% of dose.
- Continuous renal replacement therapy (CRRT): Administer 75% of dose.

-Carlson, 2005: Oral (for melphalan-prednisone combination therapy; based on a study evaluating toxicity with melphalan dosed at 0.25 mg/kg/day for 4 days/cycle):
- Cl_{cr} >10 to <30 mL/minute: Administer 75% of dose
- Cl_{cr} ≤10 mL/minute: Data is insufficient for a recommendation

-Kintzel, 1995:
-Oral: Adjust dose in the presence of hematologic toxicity
-I.V.:
- Cl_{cr} 46-60 mL/minute: Administer 85% of normal dose.
- Cl_{cr} 31-45 mL/minute: Administer 75% of normal dose.
- Cl_{cr} <30 mL/minute: Administer 70% of normal dose.

-Badros, 2001: I.V.: Autologous stem cell transplant (single-agent conditioning regimen; no busulfan or irradiation): Serum creatinine >2 mg/dL: Reduce dose from 200 mg/m^2 over 2 days (as 100 mg/m^2/day for 2 days) to 140 mg/m^2 given as a single-dose infusion

Hepatic Impairment:
Melphalan is hepatically metabolized; however, dosage adjustment does not appear to be necessary (King, 2001).

Dosing: Obesity

ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer

*(**Note:** Excludes HSCT dosing):* Utilize patient's actual body weight (full weight) for calculation of body surface area- or weight-based dosing, particularly when the intent of therapy is curative; manage regimen-related toxicities in the same manner as for nonobese patients; if a dose reduction is utilized due to toxicity, consider resumption of full weight-based dosing with subsequent cycles, especially if cause of toxicity (eg, hepatic or renal impairment) is resolved (Griggs, 2012).

Dosing: Adjustment for Toxicity

-Oral:

- WBC <3000/mm^3: Withhold treatment until recovery
- Platelets <100,000/mm^3: Withhold treatment until recovery

-I.V.: Adjust dose based on nadir blood cell counts

Common side effect :

Gastrointestinal: Nausea/vomiting, diarrhea, oral ulceration

Hematologic: Myelosuppression, leukopenia (nadir: 14-21 days; recovery: 28-35 days), thrombocytopenia (nadir: 14-21 days; recovery: 28-35 days), anemia

Miscellaneous: Secondary malignancy (<2% to 20%; cumulative dose and duration dependent, includes acute myeloid leukemia, myeloproliferative syndrome, carcinoma)

1% to 10%: Miscellaneous: Hypersensitivity (I.V.: 2%; includes bronchospasm, dyspnea, edema, hypotension, pruritus, rash, tachycardia, urticaria)

Pregnancy category: D