"Temozide®"

Generic name:

Temozolomide

Category:

Antineoplastic

Indication:

Newly diagnosed glioblastoma multiforme (GBM), Refractory anaplastic astrocytoma, Metastatic melanoma.

Mechanism of action:

Temozolomide is not directly active, but is rapidly converted at physiologic pH to the active form, MTIC[1]. MTIC alkylates DNA at the O^6 and N^7 position of guanine.

Pharmacokinetics:

Absorption:

Temozolomide is rapidly and completely absorbed after oral administration. Food reduces the rate and extent of absorption.

Distribution:

Temozolomide has a mean apparent volume of distribution (Vd is 0.4 L/kg), Weakly bound to plasma proteins (15%).

Metabolism:

Spontaneously hydrolized to active specious, MTIC, temozolomide acid metabolite. CYP-450 plays only a minor role in the metabolism of temozolomide's active metabolites.

Elimination:

About 38% of the administered drug is recovered in the urine and 1% in the feces.

Half-life:

1 . 5-(3-methyltriazen-1-yl)imidazole-4- carboxamide

The half-life is 1.8 h. Overall Clearance is approximately 5.5 L/h/m^2. The elimination half-life is similar in adults and children.

Time to peak plasma concentration: 1 hour, doubles when administered after a high fat meal.

Pregnancy:

FDA pregnancy category: D

Breast-feeding:

It is unknown whether Temozolomide is excreted in human milk; however, breastfeeding is not recommended during treatment due to potential risk to the infant.

Pediatrics:

Safety and effectiveness in pediatric patients have not established.

Drug/ Food interactions and/or related problems:

- Valproic acid: Valproic acid decreases Temozolomide clearance by about 5%.
- Vaccines (live and inactivated): because normal defense mechanisms may suppressed by Temozolomide therapy, the patient's antibody response to the vaccine may be decreased. Immunization of these patients should be undertaken only with extreme caution after careful review of patient's hematologic status and only with the knowledge and consent of physician managing the Temozolomide therapy.
- Fingolimod: Concomitant therapy is expected to increase the risk of immunosuppression.
- Food: Food reduces the extent of absorption.

Medical considerations/contraindications:

Except under special circumstances, this medication should not be used when the following medical problem exists:

Hypersensitivity to dacarbazine, temozolomide or to any of its components.

Risk- benefit should be considered when the following medical problems exist:

Bacterial or viral Infection

Sever renal or hepatic function impairment

Previous cytotoxic drug therapy or radiation

Severe myelosuppression

Side/adverse effects:

Incidence more frequent:

Alopecia, Nausea, vomiting, Fatigue, headache, constipation, anorexia, Lymphopenia, fever, hemiparesis, diarrhea, asthenia, dizziness, convulsion.

Patient monitoring:

Absolute neutrophil count and Complete blood count are recommended prior to treatment and at periodic intervals during treatment. Complete blood count should be performed 21 days after the first dose or within 48 hours of that day and at weekly intervals until recovery if the ANC falls below $1.5*10^9$ cells/L and the platelet count falls below $100*10^9$ cells/L; complete blood counts should be obtained weekly during concomitant Temozolomide and radiotherapy treatment.

Usual adult dose:

- Anaplastic Astrocytoma
  - ✓ Adults: 150 mg/m^2/day for 5 days; may repeat at 28-day intervals. Based on hematologic response, titrate up to target maintenance dosage of 200 mg/m^2/day for 5 days of each cycle.

- Newly Diagnosed Glioblastoma Multiforme
  - ✓ Adults Concomitant radiotherapy phase: 75 mg/m^2/day for 42 days concomitant with focal radiotherapy. The concomitant phase is usually followed by 6 cycles of maintenance therapy.
  - ✓ Maintenance phase, cycle 1: 150 mg/m^2/day for 5 days followed by 23 days without treatment.

- ✓ Maintenance phase, cycles 2 through 6: Escalate dosage to 200 mg/m^2/day if CTC[2] nonhematological toxicity for cycle 1 is grade 2 or less (except for alopecia, nausea, vomiting), ANC is at least 1500/mcL and platelets are at least 100000/mcL. Dosage remains at 200 mg/m^2/day for first 5 days of each subsequent cycle, except if toxicity occurs. If dose is not escalated at cycle 2, escalation should not be done in subsequent cycles.

- Take temozolomide on an empty stomach, at least 1 hour before or 2 hours after a meal. Swallow the temozolomide capsule whole, with a full glass of water.

How supplied:

Temozolomide is available as 20, 100 and 250 mg capsules in box of 5 capsules.

Storage:

Store between 15 to 30^{o}C, protect from light and moisture.

Keep out of the reach of children.

2 .Cultured T Cells