DHNP Hydroxyurea Capsule

[COMPOSITION]
Each capsule contains Hydroxyurea (USP)---------- 500 mg

[DESCRIPTION]
Each capsule, with green-colored cap and pink-colored body is filled with white colored powder.

[PHARMACOLOGICAL PROPERTIES]
Hyrdoxyurea is an orally active antineoplastic agent. Although the mechanism of action has not yet been clearly defined, hydroxyurea appears to act by interfering with synthesis of DNA. After oral administration hydroxylurea is readily absorbed from the gastrointestinal tract. Peak plasma concentrations are reached in 2 hours; by 24 hours the serum concentrations are virtually zero. Approximately 80% of an oral or intravenous dose of 7 to 30 mg/kg may be recovered from the urine within 12 hours. Hydroxyurea crosses the blood-brain barrier. Hydroxyurea is well distributed throughout the body.

[INDICATIONS]
Melanoma, resistant chronic myelocytic leukemia, and recurrent, metastatic, or inoperable carcinoma of the ovary. Hydroxyurea used concomitantly with irradiation therapy is intended for use in the local control of primary squamous cell (epidermoid) carcinomas of the head and neck, excluding the lip.

[DOSAGE & ADMINISTRATIONS]
All dosage should be based on the patient's actual or ideal weight, whichever is less.
1) SOLID TUMOR
Intermittent therapy 80 mg/kg administered orally as a single dose every third day.
Continuous Therapy 20 to 30 mg/kg administered orally as a single dose daily.
The intermittent dosage schedule offers the advantage of reduced toxicity since patients on this dosage regimen have rarely required complete discontinuance of therapy because of toxicity.
Concomitant Therapy- 80 mg/kg administered orally as a single dose every third day.
- Administration of hydroxyurea should be begun at least seven days before initiation of irradiation and continued during radiotherapy as well as indefinitely afterwards provided that the patient may be kept under adequate observation and evidences no unusual or severe reactions.
- Adjustment of irradiation dosage is not usually necessary when hydroxyurea is used concomitantly.
2) RESISTANT CHRONIC MYELOCYTIC LEUKEMIA
Until the intermittent therapy regimen has been evaluated, continuous therapy (20-30 mg/kg administered orally as a single dose daily) is recommended.

[CONTRAINDICATION:]
1)Patients with marked bone marrow depression, ie, leukopenia (< 2500 WBC/mm^3) or thrombocytopenia (< 100,000/mm^3).
2) Patients with severe anemia.

[PRECAUTION/WARNING:]
1) Treatment with hydroxyurea should not be initiated if bone marrow function is markedly depressed.
(Bone marrow suppression may occur, and leukopenia is generally its first and most common manifestation. Thrombocytopenia and anemia occur less often, and are seldom seen without a preceding leukopenia.)
2) It should be borne in mind that bone marrow depression is more likely in patients who have previously received radiotherapy of cytotoxic cancer chemotherapeutic agents; hydroyurea should be used cautiously in such patients.
3) Patients who have received irradiation therapy in the past may have an exacerbation of postirradiationerythema.
4) Severe anemia must be corrected with whole blood replacement before initiating therapy with hydroxyurea.
5) Hydroxyurea should be used with caution in patients with marked renal dysfunction.
6) Elderly patients may be more sensitive to the effects of hydroxyurea, and may require a lower dose regimen.
7) Interstitial lung disease including pulmonary fibrosis, lung infiltration, pneumonitis, and alveolitis/allergic alveolitis have been reported in patients treated for myeloproliferative neoplasm and may be associated with fatal outcome. Patient developing pyrexia, cough, dyspnoea or other respiratory symptoms should be closely monitored, investigated and treated. Promptly discontinue hydroxyurea and treatment with corticosteroids appears to be associated with resolution of the pulmonary events.

[General precautions]
1) Therapy with hydroxyurea requires close supervision. The complete status of the blood, including bone marrow examination, if indicated, as well as kidney function and liver function should be determined prior to, and repeatedly during, treatment. The determination of the hemoglobin level, total leukocyte counts, and platelet counts should be performed at least once a week throughout the course of hydroxyurea therapy. If the white blood cell count decreases to less than 2500/mm^3, or the platelet count to less than 100,000/mm^3, therapy should be interrupted until the values rise significantly toward normal levels. Anemia, if it occurs, should be managed with whole blood replacement, without interrupting hydroxyurea therapy.
2) Patients who take the drug by emptying the contents of the capsule into water should be reminded that this is a potent medication that must be handled with care. Patients must be cautioned not to allow the powder to come in contact with the skin or mucous membranes.
3) Pain or discomfort from inflammation of the mucous membranes at the irradiated site (mucositis) is usually controlled by measures such as topical anesthetics and orally administered analgesics.
If the reaction is severe, hydroxyurea therapy may be temporarily interrupted; if it is extremely severe, irradiation dosage may, in addition, be temporarily postponed. However, it has rarely been necessary to terminate these therapies.
4) Erythrocytic abnormalities: Megaloblastic erythropoiesis which is self-limiting, is often seen early in the course of hydroxurea therapy. The morphologic change resembles that seen in pernicious anema, but is not related to vitamin B12 or folic acid deficiency. The macrocytosis may mask the incidental development of folic acid deficiency; thus, prophylactic administration of folic acid may be warranted. Hydroxyurea mayalso delay plasma iron clearance and reduce the rate of iron utilization by erythrocytes, but is does not appear to alter the red blood cell survival time. Patients who have received irradiation therapy in the past may have an exacerbation of postirradiation erythema when hydroxyurea is given.
5) Sickle cell anemia: Patient with sickle cell anemia being treated with DHNP Hydroxyurea must be monitored closely for evidence for worsening anemia.
6) Secondary leukemia: In patients receiving long-term therapy with hydorxyurea for myeloproliferative disorders, secondary leukemia has been reported
7) Paediatrics use: Because of the rarity of carcinomas of the head and neck in children, dosage regimens have not been established. Also, safety and effectiveness in children have not been established.
8) The effect of DHNP hydroxyurea on driving and operating machinery has not been studied. Since DHNP hydroxyurea may cause drowsiness and other neurologic effects, alertness may be impaired

Use in pregnancy: Drugs which affect DNA synthesis, such as hydroxyurea, may be potential mutagenic agents. The physician should carefully consider this possibility before administering this drug to male or female patients who may contemplate conception. Hydroxyurea is a known teratogenic agent in animals.
Therefore, hydroxyurea should not be used in women who are or may become pregnant unless in the judgment of the physician the potential benefits outweigh the possible hazards.

Nursing Mothers: Hydroxyurea is excreted in human milk. Because of the potential for serious adverse reactions with hydroxyurea, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

[ADVERSE REACTIONS]
1) Psychoneural system: Rarely, headache, dizziness, disorientation, hallucinations, and convulsions may be caused.
2) Gastrointestinal: Stomatitis, inappetence, nausea, vomiting, diarrhea, and constipation may occur.
3) Hematologic: Primarily, bone marrow depression (leukopenia, anemia, thrombocytopenia) may occur.
Megaloblastic erythropoiesis, which is self-limiting, is often seen early in the course of hydroxyurea therapy.
4) Urogenital system: Dysuria occur very rarely. Hydroxyurea occasionally may cause temporary impairment of renal tubular function accompanied by elevations in serum uric acid, BUN, and creatinine levels.
5) Central Nervous System: At the higher dose, general lethargy state may be caused, and flush, chill, malaise have been reported.
6) Dermatologic: Occasionally, maculopapular rash, facial erythema may occur.
7) Hepatic: Abnormal BSP retention, elevation of hepatic enzymes have been reported.
8) Other: Very rare alopecia may be caused.
9) Adverse reactions observed with combined DHNP hydroxyurea and irradiation therapy were similar to those reported with the use of DHNP hydroxyurea alone, primarily bone marrow depression (leucopenia and anemia) and gastric irritation
10) Respiratory, Thoracic, and Mediastinal Disorders: Interstitial lung disease (unknown frequency)

[OVERDOSE]
Immediate treatment consists of gastric lavage, followed by supportive therapy for the cardiorespiratory systems if required. In the long term, careful monitoring of the haemopoietic system is essential and, if Necessary, blood should be transfused. Acute mucocutaneous toxicity has been reported in patients receiving hydroxyurea at a dosage several times greater than that recommended. Soreness, violet erythema, oedema on palms and foot soles followed by scaling of hands and feet, intense generalized hyperpigmentation of skin, and severe acute stomatitis were observed.

[DRUG INTERACTIONS]
The myelosuppressieve activity may be potentiated by previous or concomitant radiotherapy or cytotoxic therapy.
Since hydroxyurea may raise the concentration or blood uric acid, dosage adjustment of antigout agents may be necessary to control hyperuricemia and gout. Allopurinol may be preferred to prevent or reverse hydroxyurea induced hyperuricemia because of risk of uric acid nepropathy with uricosuric antigout agents.
Leukopenia and/or thrombocytopenia effects of hydroxyurea may be increased with concurrent or recent therapy if "blood dyscrasia - causing medications" cause the same effects. Dosage adjustment of hydroxyurea, if necessary, should be based on blood counts.
Concurrent use with a live virus vaccine may potentiate the replication of the vaccine virus, may increase the adverse effects of the vaccine virus, and /or may decrease the patient's antibody response to the vaccine.

[STORAGE] Preserve in well-closed containers. Store below 30℃, protected from light.
[PACKAGE] Blister pack of 10 x 10's / Box
[SHELF LIFE] 3 years

Manufactured by
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100 X 280 mm

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