Monitor blood counts at least once a week during hydroxyurea therapy.

Hydroxyurea is a cytotoxic drug. Follow applicable special handling and disposal procedures. (see Reference) Antiretroviral drugs may reduce the adverse effects of hydroxyurea; discontinue hydroxyurea capsules and consider alternative therapy if this occurs. (5.3, 7.3)

To report SUSPECTED ADVERSE REACTIONS, contact Par Pharmaceutical at 1-800-825-3103 or FDA at 1-800-FDA-1088 or fda.gov/medwatch

Use in Specific Populations

Pregnancy: Hydroxyurea is a human carcinogen. In patients receiving long-term hydroxyurea for myeloproliferative disorders, secondary leukemias have been reported. Skin cancer has also been reported in patients receiving long-term hydroxyurea. Advise protection from sun exposure and re- sistance for the development of secondary malignancies.

Embryo-Fetal Toxicity: Hydroxyurea is a human teratogen. Advise pregnant women to use effective contraception. Provide education about the potential risk to a fetus and use of effective contraception. (5.3)

Criteria for Termination: In patients taking hydroxyurea capsules, male patients should not father children during and after treatment with hydroxyurea capsules for at least 1 year after therapy. (5.3, 8.1)

Vasculitic Toxicities: Cutaneous vasculitic toxicities, including vesicular ulcerations and gangrene, have occurred in patients with myeloproliferative disorders during therapy with hydroxyurea. These vasculitic toxicities were reported most often in patients with a history of, or currently receiving, immunosuppressive therapy. If cutaneous vasculitic ulcers occur, initiated treatment and discontinue hydroxyurea capsules. (5.2, 5.3)

Live Vaccinations: Avoid live vaccine use in a patient taking hydroxyurea capsules. Vaccination with live vaccines in a patient receiving hydroxyurea capsules may result in severe infection. Patient's antibody response to vaccines may be decreased. Consider consultation with a specialist. (5.3, 8.1)

Risks with concomitant use of antiretroviral drugs: Data in patients taking hydroxyurea capsules and antiretroviral drugs, including didanosine and stavudine, indicate that the potential risk to a fetus and use of effective contraception may be increased. (5.3, 7.3)

Radiation Recall: Patients who have received irradiation therapy in the past may have increased risk of radiation recall. If cutaneous vasculitic ulcers occur, initiate treatment and discontinue hydroxyurea capsules. (5.3, 5.4)

Skin cancer has also been reported in patients receiving long-term hydroxyurea for myeloproliferative disorders, secondary leukemias have been reported. Skin cancer has also been reported in patients receiving long-term hydroxyurea. Advise protection from sun exposure and resistance for the development of secondary malignancies.

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Hydroxyurea capsules can cause fetal harm based on findings from animal reproduction studies. Hydroxyurea may damage spermatozoa and testicular tissue, resulting in azoospermia or infertility. Based on findings in animals and humans, male fertility may be compromised by treatment with hydroxyurea capsules. Azoospermia or infertility after therapy. Advise females to immediately report pregnancy.

Hydroxyurea capsules may damage spermatogenesis and testicular tissue, resulting in azoospermia or infertility. Male with female sexual partners of reproductive potential should use effective contraception. There are no data on the effect of food on the absorption of hydroxyurea.

Hydroxyurea is a hydrazine that inhibits DNA synthesis by binding to DNA polymerase, thereby preventing DNA replication and cell growth. This mechanism is not dependent on the presence of thymine dimer and is therefore not subject to the normal repair process of cells damaged but not killed by irradiation.

In humans, hydroxyurea can cause significant hematologic toxicity, including leukopenia, thrombocytopenia, and anemia. The severity and duration of these effects are dose-dependent and can be prevented by the administration of folic acid.

The hematologic toxicity of hydroxyurea is dose-dependent and time-dependent. The hematopoietic system is fully recovered following drug cessation; however, the recovery may take longer in patients receiving higher doses or more frequent dosing. The hematologic effects of hydroxyurea can be reversed by the administration of folic acid, which competes with hydroxyurea for uptake by cells.

Hydroxyurea is rapidly absorbed following oral administration, with peak plasma concentrations occurring within 1-2 hours. The drug is extensively metabolized in the liver, with less than 10% of the dose excreted unchanged in the urine.

Hydroxyurea may cross the placenta and have been associated with a variety of adverse effects in the newborn. The drug is excreted in human milk, and breastfeeding is not recommended during hydroxyurea therapy.