Xelobine®

Capecitabine USP

Presentation

Xelobine® 500 mg tablet: Each film-coated tablet contains Capecitabine USP 500 mg.

Description

Capecitabine is a fluoropyrimidine carbamate with antineoplastic activity. It is an orally administered systemic prodrug of 5'-deoxy-5-fluorouridine (5'-DFUR) which is converted to 5-fluorouracil.

Pharmacodynamics/ Pharmacokinetics

Mechanism of Action

Enzymes convert capecitabine to 5-fluorouracil (5-FU) in vivo. Both normal and tumor cells metabolize 5-FU to 5-fluoro-2'-deoxyuridine monophosphate (FdUMP) and 5-fluorouridine triphosphate (FUTP). These metabolites cause cell injury.

Absorption

Following oral administration of 1255 mg/m^2 BID to cancer patients, Capecitabine reached peak blood levels in about 1.5 hours (Tmax).

Distribution

Plasma protein binding of capecitabine and its metabolites is less than 60% and is not concentration-dependent.

Bioactivation and Metabolism

Capecitabine is extensively metabolized enzymatically to 5-FU. In the liver, a 60 kDa carboxylesterase hydrolyzes much of the compound to 5'-deoxy-5-fluorocytidine (5'-DFCR). Cytidine deaminase, an enzyme found in most tissues, including tumors, subsequently converts 5'-DFCR to 5'-DFUR. The enzyme, thymidine phosphorylase (dThdPase), then hydrolyzes 5'DFUR to the active drug 5-FU.

Excretion

Capecitabine and its metabolites are predominantly excreted in urine; 95.5% of administered capecitabine dose is recovered in urine.

Indications

Adjuvant Colon Cancer

- Patients with Dukes' C colon cancer

Metastatic Colorectal Cancer

- First-line as monotherapy when treatment with fluoropyrimidine therapy alone is preferred

Metastatic Breast Cancer

- In combination with docetaxel after failure of prior anthracycline containing therapy
- As monotherapy in patients resistant to both paclitaxel and an anthracycline-containing regimen

Dosage and administration

Monotherapy (Metastatic Colorectal Cancer, Adjuvant Colorectal Cancer, Metastatic Breast Cancer):

The recommended dose of Capecitabine is 1250 mg/m^2 administered orally twice daily (morning and evening; equivalent to 2500 mg/m^2 total daily dose) for 2 weeks followed by a 1-week rest period given as 3-week cycles.

Adjuvant treatment in patients with Dukes' C colon cancer is recommended for a total of 6 months ie, Capecitabine 1250 mg/m^2 orally twice daily for 2-weeks followed by a 1-week rest period, given as 3-weeks cycles for a total of 8 cycles (24 weeks)

In Combination With Docetaxel (Metastatic Breast Cancer):

In combination with docetaxel, the recommended dose of Capecitabine is 1250 mg/m^2 twice daily for 2 weeks followed by a 1-week rest period, combined with docetaxel at 75 mg/m^2 as a 1-hour intravenous infusion every 3 weeks.

Use in specific populations

Pregnancy: Pregnancy Category D.
Can cause fetal harm. Advise women of the potential risk to the fetus.
Nursing Mothers: Discontinue nursing when receiving Capecitabine treatment.
Geriatric: Greater incidence of adverse reactions. Monitoring required.

Contraindications

Capecitabine is contraindicated in patients with known hypersensitivity to Capecitabine or to any components of its and severe renal impairment.

Warnings and precautions

Coagulopathy: May result in bleeding, death. Monitor anticoagulant response (e.g., INR) and adjust anticoagulant dose accordingly.
Diarrhea: May be severe. Interrupt Capecitabine treatment immediately until diarrhea resolves or decreases to grade 1. Recommend standard antidiarrheal treatments.
Cardiotoxicity: Common in patients with a prior history of coronary artery disease.
Dehydration and Renal Failure: Interrupt Capecitabine treatment until dehydration is corrected. Potential risk of acute renal failure secondary to dehydration. Monitor and correct dehydration.
Mucocutaneous and Dermatologic Toxicity: Severe mucocutaneous reactions, Steven-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), have been reported.
Hyperbilirubinemia: Interrupt Capecitabine treatment immediately until the hyperbilirubinemia resolves or decreases in intensity.
Hematologic: Do not treat patients with neutrophil counts $<1.5 \times 10^9$/L or thrombocyte counts $<100 \times 10^9$/L. If grade 3-4 neutropenia or thrombocytopenia occurs, stop therapy until condition resolves.

Adverse reactions

Most common adverse reactions (30%) were diarrhea, hand-and-foot syndrome, nausea, vomiting, abdominal pain, fatigue/weakness, and hyperbilirubinemia.

Drug interactions

Anticoagulants: Monitor anticoagulant response (INR or prothrombin time) frequently in order to adjust the anticoagulant dose as needed.
Phenytoin: Monitor phenytoin levels in patients taking Capecitabine concomitantly with phenytoin. The phenytoin dose may need to be reduced.
Leucovorin: The concentration of 5-fluorouracil is increased and its toxicity may be enhanced by leucovorin.

Overdosage

The manifestations of acute overdose would include nausea, vomiting, diarrhea, gastrointestinal irritation and bleeding, and bone marrow depression. Medical management of overdose should include customary supportive medical interventions aimed at correcting the presenting clinical manifestations. Although no clinical experience using dialysis as a treatment for Capecitabine overdose has been reported, dialysis may be of benefit in reducing circulating concentrations of 5'-DFUR, a low molecular-weight metabolite of the parent compound. Single doses of Capecitabine were not lethal to mice, rats, and monkeys at doses up to 2000 mg/kg.

Storage

Store at temperature not exceeding 30°C in a dry place. Protect from light and moisture.

Packaging

Xelobine® 500 tablet: Each commercial box contains 30 tablets in Alu-Alu blister pack.

Medicine: Keep out of reach of children

For further information, please contact: 01977 158 926
(9.00 am - 5.00 pm)

Healthcare

Manufactured by
Healthcare Pharmaceuticals Ltd.
Rajendrapur, Gazipur, Bangladesh

HP 52341