Capecitin

Capecitabine USP

COMPOSITION

Capecitin 500 mg Tablet: Each film coated tablet contains Capecitabine USP 500 mg.

CLINICAL PHARMACOLOGY

Mechanism of action: 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 (5-FU) by in vivo enzymatic conversion. 5-FU is then metabolized to 5-fluoro-2'-deoxyuridine monophosphate (FdUMP) and 5-fluorouridine triphosphate (FUTP) by both normal and tumor cells, and these metabolites cause cell injury by inhibiting DNA synthesis, RNA processing and protein synthesis.

Pharmacokinetics: ***Absorption:*** After oral administration, Capecitabine is rapidly and extensively absorbed followed by extensive conversion to the metabolites; administration with food decreases the rate of Capecitabine absorption. ***Distribution:*** Plasma protein binding of Capecitabine and its metabolites is less than 60% and is not concentration-dependent. ***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), which is then converted to 5'-DFUR by cytidine deaminase, an enzyme found in most tissues, including tumors. An 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. Fecal excretion is minimal (2.6%). About 3% of the administered dose is excreted in urine unchanged.The elimination half-life of both Capecitabine and 5-FU is about 0.75 hour.

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): 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, given as 1250 mg/m^2 orally twice daily for 2 weeks followed by a 1-week rest period, as 3-week cycles for a total of 8 cycles (24 weeks).

In Combination with Docetaxel (Metastatic Breast Cancer): The recommended dose 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.

Capecitin tablets should be swallowed whole with water within 30 minutes after a meal. Do not crush or cut Capecitin tablets. Dose is calculated according to body surface area.

CONTRAINDICATIONS

Capecitin is contraindicated in patients with known hypersensitivity to Capecitabine and patients who have a known hypersensitivity to 5 fluorouracil. It is also contraindicated in patients with severe renal impairment (creatinine clearance below 30 mL/min).

SIDE EFFECTS

The most common side effects of Capecitabine include diarrhoea, hand and foot syndrome, nausea, vomiting, stomach-area (abdominal) pain, tiredness, weakness.

PRECAUTIONS

Pregnancy: Pregnancy category D. Capecitabine can cause fetal harm when administered to a pregnant woman.Women should be advised to avoid becoming pregnant while receiving treatment with Capecitabine. **Nursing mothers:** Because of the potential for serious adverse reactions in nursing infants from Capecitabine, 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. **Pediatric use:** The safety and effectiveness of Capecitabine in pediatric patients have not been established. **Geriatric Use:** It is required to pay particular attention in monitoring the adverse effects of Capecitabine in the elderly. **Hepatic Insufficiency:** Caution should be exercised when patients with mild to moderate hepatic dysfunction due to liver metastases are treated with Capecitabine. **Coagulopathy:** May result in bleeding, death. Monitor anticoagulant response (e.g. INR) and adjust anticoagulant dose accordingly. **Diarrhoea:** May be severe. Interrupt Capecitabine treatment immediately until diarrhoea resolves or decreases to grade 1. Recommend standard anti diarrhoeal treatments. **Cardiotoxicity:** Common in patients with a prior history of coronary artery disease. **Dehydration and Renal Failure:** Potential risk of acute renal failure secondary to dehydration. Interrupt Capecitabine treatment until dehydration is corrected. **Mucocutaneous and Dermatologic Toxicity:** Severe mucocutaneous reactions, Steven-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) have been reported. Capecitabine should be permanently discontinued in patients who experience a severe mucocutaneous reaction during treatment. **Hyperbilirubinemia:** Interrupt Capecitabine treatment immediately until the hyperbilirubinemia resolves or decreases in intensity. **Hematologic:** Do not treat patients with neutrophil counts <1.5x10^9/L or thrombocyte counts <100x10^9/L. If grade 3-4 neutropenia or thrombocytopenia occurs, stop therapy until condition resolves.

DRUG INTERACTIONS

Drug-Drug Interactions: ***Anticoagulants:*** Altered coagulation parameters and/or bleeding have been reported in patients taking Capecitabine concomitantly with coumarin-derivative anticoagulants such as warfarin and phenprocoumon, monitor anticoagulant response (INR or prothrombin time) frequently in order to adjust the anticoagulant dose as needed. ***Phenytoin:*** Capecitabine may cause toxicity associated with elevated phenytoin levels, 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. ***CYP2C9 substrates:*** Care should be exercised when Capecitabine is co-administered with CYP2C9 substrates.

OVERDOSE

Acute overdose of Capecitabine may cause nausea, vomiting, diarrhoea, 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.

STORAGE

Store below 30°C. Keep in a dry place away from light.

PRESENTATION

Capecitin 500 mg Tablet: Each box contains 3X10 Capecitin tablets in Alu-Alu blister pack.

Manufactured for:
ARISTOPHARMA LTD.
Shampur-Kadamtali I/A, Dhaka-Bangladesh
by Healthcare Pharmaceuticals Limited, Rajendrapur, Gazipur

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