Front

For the use only of Registered Medical Practitioner or a Hospital or a Laboratory.

CAPECITABINE TABLETS IP 500 mg

CABITA™ 500

Antineoplastic agent

COMPOSITION

CABITA™500

Each film coated tablet contains:

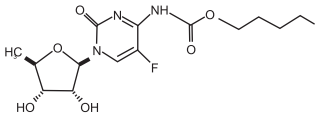
Capecitabine IP	500 mg
Excipients	q.s

Colour: Red Oxide of Iron and Titanium Dioxide

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.

The chemical name for capecitabine is 5'-deoxy-5-fluoro-N-[(pentyloxy) carbonyl]- cytidine and has a molecular weight of 359.35. Capecitabine has the following structural formula:



CLINICAL PHARMACOLOGY

Capecitabine is relatively non-cytotoxic in vitro. This drug is enzymatically converted to 5-fluorouracil (5-FU) in vivo.

Bioactivation

Capecitabine is readily absorbed from the gastrointestinal tract. 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'-deoxy-5-fluorouridine (5'-DFUR).

Mechanism of Action

The mechanism of action of Capecitabine are by two different mechanism First, FdUMP and the folate cofactor, N5-10-methylenetetrahydrofolate, bind to thymidylate synthase (TS) to form a covalently bound ternary complex. This binding inhibits the formation of thymidylate from 2'-deoxyuridylate. Thymidylate is the necessary precursor of thymidine triphosphate, which is essential for the synthesis of DNA, so that a deficiency of this compound can inhibit cell division. Second, nuclear transcriptional enzymes can mistakenly incorporate FUTP in place of uridine triphosphate (UTP) during the synthesis of RNA. This metabolic error can interfere with RNA processing and protein synthesis.

INDICATIONS

Colorectal Cancer

Capecitabine is indicated as a single agent for adjuvant treatment in patients with Dukes' C colon cancer who have undergone complete resection of the primary tumor when treatment with fluoropyrimidine therapy alone is preferred.

Breast Cancer

Capecitabine in combination with docetaxel is indicated for the treatment of patients with metastatic breast cancer after failure of prior anthracycline containing chemotherapy.

DOSAGE AND ADMINISTRATION

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. Capecitabine tablets should be swallowed with water within 30 minutes after a meal. 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. Pre-medication, according to the docetaxel labeling, should be started prior to docetaxel administration for patients receiving the Capecitabine plus docetaxel combination.

Adjustment of Starting Dose in Special Populations

Hepatic Impairment

In patients with mild to moderate hepatic dysfunction due to liver metastases, no starting dose adjustment is necessary; however, patients should be carefully monitored.

Renal Impairment

No adjustment to the starting dose of Capecitabine is recommended in patients with mild renal impairment (creatinine clearance = 51 to 80 ml/min. In patients with moderate renal impairment (baseline creatinine clearance = 30 to 50 ml/min), a dose reduction to 75 % of the Capecitabine starting dose when used as monotherapy or in combination with docetaxel (from 1250 mg/m^2 to 950 mg/m^2 twice daily) is recommended.

Geriatrics

Physicians should exercise caution in monitoring the effects of Capecitabine in the elderly. Insufficient data are available to provide a dosage recommendation.

PRECAUTIONS

Patients receiving therapy with Capecitabine should be monitored by a physician experienced in the use of cancer chemotherapeutic agents. Most adverse events are reversible and do not need to result in discontinuation, although doses may need to be withheld or reduced.

Cardiotoxicity

The cardiotoxicity observed with Capecitabine includes myocardial infarction/ischemia, angina, dysrhythmias,cardiac arrest, cardiac failure, sudden death, electrocardiographic changes, and cardiomyopathy. These adverse events may be more common in patients with a prior history of coronary artery disease.

SIDE EFFECTS

Hematological: Neutropenia and thrombocytopenia occur in approximately 20 % of patients, while anemia is observed in approximately 14 %.

Gastrointestinal: Diarrhea is common (50 %) may be severe and require clinical management (e.g. Hydration, electrolyte replacenment). Other gastrointestinal side effects include nausea (40 %), vomiting, stomatitis, constipation, abdominal pain, dysepia, anorexia and dehydration.

Dermatological: Hand and foot syndrome (i.e. palmar-plantar erythrodysesthesia or acral erthema) occurs in up to 50% of patients. Signs and symptoms include numbness, dysesthesia/paresthesia, tingling, painless or painful swelling, erythema, desquamation, blistering and pain. If grade 2 or 3 toxicity occurs, it is recommended that treatment be discontinued until symptoms resolve to at least grade 1.

Hepatic Hyperbilirubinemia (17 %), increased alkaline phosphatase, increased hepatic transaminases.

Neurological Paresthesias, headace, dizziness and insomnia are most common.

Less commonly observed are confusion, ataxia, encephalopathy and altered state of consciousness.

Cardiovascular, EKG changes, myocardial infarction, angina pectoris, cardiomyopathy, hypotension, hypertension. These side effects are more commonly seen in patients with a previous cardiac history.

Other: Eye irritation, fatigue, edema, fever, muscle aches.

Hepatic Insufficiency

Patients with mild to moderate hepatic dysfunction due to liver metastases should be carefully monitored when Capecitabine is administered. The effect of severe hepatic dysfunction on the disposition of Capecitabine is not known

OVERDOSE

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.

CONTRAINDICATIONS

Capecitabine is contraindicated in patients with known hypersensitivity to capecitabine or to any of its components. Capecitabine is contraindicated in patients who have a known hypersensitivity to 5-fluorouracil.

STORAGE

Store below 30 °C. Protect from light and moisture.

Keep out of reach of children.

PRESENTATION

CABITA™500 CapecitabineTablet IP 500 mg are available in blister pack of 10 tablets.

Marketed by:
Getwell Oncology Pvt. Ltd.
(A unit of Getwell)
464, Udyog Vihar, Phase -V,
Gurgaon -122 016, Haryana, India.

Manufactured by:
Getwell Pharmaceuticals
Vastrapur, Ahmedabad - 380015,
Gujarat, INDIA.
At: 357, GIDC, Sachin, Surat, Gujarat, INDIA

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