Kaneva®

Erlotinib
Tablet

Description
Kaneva® is a preparation of Erlotinib, which is a type of biological therapy called a tyrosine kinase inhibitor (TKI). It works by blocking particular proteins on cancer cells that encourage the cancer to grow. Erlotinib blocks proteins called epidermal growth factor receptors (EGFR). Cancers that have these receptors called EGFR positive. Erlotinib may shrink the cancer or stop it growing for a time.

Mode of Action
Erlotinib is an epidermal growth factor receptor/human epidermal growth factor receptor type 1 (EGFR also known as HER1) tyrosine kinase inhibitor. Erlotinib potently inhibits the intracellular phosphorylation of EGFR. EGFR is expressed on the cell surface of normal cells and cancer cells. In non-clinical models, inhibition of EGFR phosphotyrosine results in cell stasis and/or death.
EGFR mutations may lead to constitutive activation of anti-apoptotic and proliferation signaling pathways. The potent effectiveness of erlotinib in blocking EGFR-mediated signalling in these EGFR mutation positive tumours is attributed to the tight binding of erlotinib to the ATP-binding site in the mutated kinase domain of the EGFR. Due to the blocking of downstream-signaling, the proliferation of cells is stopped, and cell death is induced through the intrinsic apoptotic pathway. Tumour regression is observed in mouse models of enforced expression of these EGFR activating mutations.

Indication and Usage
• First-line treatment of patients with metastatic Non-Small Cell Lung cancer (NSCLC) whose tumors have Epidermal Growth Factor Receptor (EGFR) exon 19 deletions or exon 21 substitution mutations as detected.
• Maintenance treatment of patients with locally advanced or metastatic NSCLC whose disease has not progressed after four cycles of platinum based first-line chemotherapy.
• Treatment of locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen.
• First-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer, in combination with gemcitabine.

Dosage & Administration
• The dose for NSCLC is 150 mg/day.
• The dose for pancreatic cancer is 100 mg/day.
• All doses of Kaneva® should be taken on an empty stomach at least one hour before or two hours after ingestion of food.
• Reduce in 50 mg decrements, when necessary.

Warning and Precautions
• Interstitial Lung Disease (ILD)-like events, including fatalities have been infrequently reported. Kaneva® should be stopped if acute onset of new or progressive unexplained pulmonary symptoms, such as dyspnea, cough and fever occur. Kaneva® should be discontinued if ILD is diagnosed.
• Cases of acute renal failure (including fatalities), and renal insufficiency have been reported. Interrupt Kaneva® in the event of dehydration. Monitor renal function and electrolytes in patients at risk of dehydration.
• Cases of hepatic failure and hepatorenal syndrome (including fatalities) have been reported. Monitor periodic liver function testing. Interrupt or discontinue Kaneva® if liver function changes are severe.
• Monitor patients with hepatic impairment closely. Kaneva® should be stopped if changes in liver function are severe.
• Gastrointestinal perforations, including fatalities, have been reported. Kaneva® should be discontinued.
• Bullous and exfoliative skin disorders, including fatalities, have been reported. Kaneva® should be discontinued.
• Myocardial infarction/ischemia has been reported, including fatalities, in patients with pancreatic cancer.
• Cerebrovascular accidents, including a fatality, have been reported in patients with pancreatic cancer.
• Microangiopathic Hemolytic Anemia with thrombocytopenia has been reported in patients with pancreatic cancer.
• Corneal perforation and ulceration have been reported. Kaneva® should be interrupted.
• International Normalized Ratio (INR) elevations and bleeding events, some associated with concomitant warfarin administration have been reported. Patients should be monitored taking warfarin or other coumarin-derivative anticoagulants.
• Kaneva® may cause fatal harm when administered to a pregnant woman. Women should be advised to avoid pregnancy while on Kaneva®.

Contraindications
Hypersensitivity to Erlotinib or to any of the excipients.

Adverse Reactions
• The most common adverse reactions (>20%) in maintenance treatment are rash-like events and diarrhea.
• The most common adverse reactions (>20%) in 2nd line NSCLC are rash, diarrhea, anorexia, fatigue, dyspnea, cough, nausea, infection and vomiting.
• The most common adverse reactions (>20%) in pancreatic cancer are fatigue, rash, nausea, anorexia, diarrhea, abdominal pain, vomiting, weight decrease, infection, edema, pyrexia, constipation, bone pain, dyspnea, stomatitis and myalgia.

Use in Specific Populations
Pregnancy: Pregnancy category D.
Based on its mechanism of action, Erlotinib can cause fetal harm when administered to a pregnant woman.
Nursing mothers
It is not known whether Erlotinib is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Erlotinib, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.
Pediatric use
The safety and effectiveness of Erlotinib in pediatric patients have not been established.
Geriatric use
No overall differences in safety or efficacy were observed between subjects 65 years and older and those younger than 66.

Drug Interactions
• CYP3A4 inhibitors may increase erlotinib plasma concentrations.
• CYP3A4 inducers may decrease erlotinib plasma concentrations.
• CYP1A2 inducers may decrease erlotinib plasma concentrations.
• Erlotinib solubility is pH dependent. Drugs that alter the pH of the upper GI tract may alter the solubility of erlotinib and hence its absorption.
• Cigarette smoking decreases erlotinib plasma concentrations.

Overdosage
Single oral doses of Erlotinib up to 1,000 mg in healthy subjects and weekly doses up to 1,600 mg in cancer patients have been tolerated. Repeated twice-daily doses of 200 mg single-agent Erlotinib in healthy subjects were poorly tolerated after only a few days of dosing. Based on the data from these studies, an unacceptable incidence of severe adverse reactions, such as diarrhea, rash, and liver transaminase elevation, may occur above the recommended dose. In case of suspected overdose, Erlotinib should be withheld and symptomatic treatment instituted.

Pharmaceutical Precautions
Keep in a dry place and store below 30° C. Protect from light and keep out of the reach of children.

Commercial Pack
Kaneva® 100 Tablet: Box containing 30 tablets in 3x10's Alu-Alu form packs. Each film coated tablet contains Erlotinib Hydrochloride INN equivalent to Erlotinib 100 mg.
Kaneva® 150 Tablet: Box containing 30 tablets in 3x10's Alu-Alu form packs. Each film coated tablet contains Erlotinib Hydrochloride INN equivalent to Erlotinib 150 mg.

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