Vandetanib

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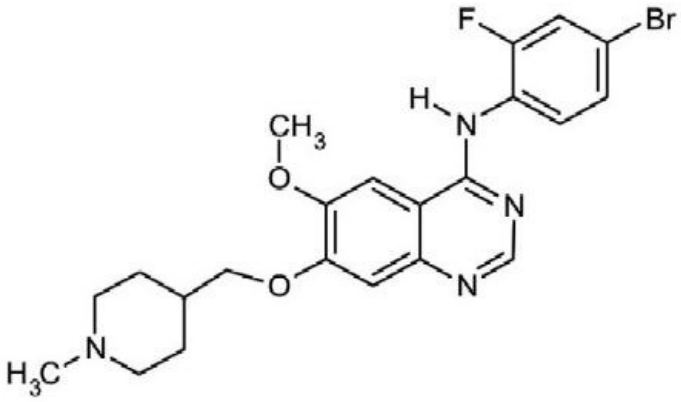

Brand name: Caprelsa®
IUPAC: N-(4-bromo-2-fluorophenyl)-6-methoxy-7-[(1-methylpiperidin-4-yl)methoxy]quinazolin-4-amine
FDA approval: Yes
Manufacturer Link
Usage:

Thyroid cancer is a cancerous growth of the thyroid gland, which is located in the neck. Medullary thyroid cancer involves specific types of cells that are found in the thyroid gland and can occur spontaneously, or be part of a genetic syndrome.

About 44,600 new thyroid cancer cases were diagnosed in the United States during 2010, and about 1,690 people died from the disease, according to the National Cancer Institute. Medullary thyroid cancer is estimated to represent 3 to 5 percent of all thyroid cancer; its estimated incidence in the United States for 2010 is about 1,300 to 2,200 patients, making it one of the rarer forms of thyroid cancer. Common symptoms of medullary thyroid cancer may include coughing, difficulty swallowing, enlargement of the thyroid gland, swelling of the neck, a lump on the thyroid, and changes in a person’s voice or hoarseness. Vandetanib targets medullary thyroid cancer’s ability to grow and expand. There are currently no FDA-approved treatments for this type of cancer. Vandetanib is administered orally on a daily basis.

The recommended daily dose is 300 mg of Vandetanib taken orally. Vandetanib treatment should be continued until patients are no longer benefiting from treatment or an unacceptable toxicity occurs. Vandetanib may be taken with or without food. If a patient misses a dose, the missed dose should not be taken if it is less than 12 hours before the next dose.

Mechanism:

Vandetanib is a tyrosine kinase inhibitor. In vitro studies have shown that Vandetanib inhibits the activity of tyrosine kinases including members of the epidermal growth factor receptor (EGFR) family, vascular endothelial cell growth factor (VEGF) receptors, rearranged during transfection (RET), protein tyrosine kinase 6 (BRK), TIE2, members of the EPH receptors kinase family, and members of the Src family of tyrosine kinases. Vandetanib inhibits endothelial cell migration, proliferation, survival and new blood vessel formation in in vitro models of angiogenesis. Vandetanib inhibits EGFR-dependent cell survival in vitro. In addition, Vandetanib inhibits epidermal growth factor (EGF)-stimulated receptor tyrosine kinase phosphorylation in tumor cells and endothelial cells and VEGF-stimulated tyrosine kinase phosphorylation in endothelial cells.

In vivo Vandetanib administration reduced tumor cell-induced angiogenesis, tumor vessel permeability, and inhibited tumor growth and metastasis in mouse models of cancer.

Side effects:

Side effects of Caprelsa include: diarrhea, rash, nausea, high blood pressure, headache, fatigue, decreased appetite, and stomach (abdominal) pain. Serious side effects reported during the study resulted in five deaths in patients treated with vandetanib. Causes of death included breathing complications, heart failure, and a bacterial infection in the blood (sepsis).