# Product Data Sheet

Product Name: Vandetanib hydrochloride
Cat. No.: GC11876

## Chemical Properties

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|---|---|---|---|
| Cas. No. | 524722-52-9 | | |
| Chemical Name | N-(4-bromo-2-fluorophenyl)-6-methoxy-7-((1-methylpiperidin-4-yl)methoxy)quinazolin-4-amine hydrochloride | | |
| SMILES | CN1CCC(COC2=C(OC)C=C(C(NC3=C(F)C=C(Br)C=C3)=NC=N4)C4=C2)CC1.Cl | | |
| Formula | $C_{22}H_{25}BrClFN_4O_2$ | M.Wt | 511.81 |
| Solubility | ≥ 51.2 mg/mL in DMSO with gentle warming | Storage | Store at -20°C |
| General tips | For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months. | | |
| Shipping Condition | Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request. | | |
| Structure | Vandetanib hydrochloride | | |

## Protocol

**Cell experiment:**

Growth inhibition is measured by a modified MTT assay. Briefly, the cells are plated on 96-well plates at a density of 2000 cells per well and exposed to each gefitinib or vandetanib for 72 h. Each assay is performed in triplicate. The 50% inhibitory concentration (IC50) of each drug is determined as the mean±standard deviation (SD).


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**Animal experiment:**

One million H1650 cells or H1650/PTEN cells (H1650 cells with a transfected PTEN gene) are injected subcutaneously into the backs of each mouse. On 10th day after injection, mice are randomLy assigned to three groups, which receive either vehicle, vandetanib (15 mg/kg/day), or gefitinib (15 mg/kg/day). Vehicle, vandetanib, and gefitinib are administered once per day p.o., five times per week. Tumor volume (width×width×length/2) and body weight are determined periodically. Tumor volumes are expressed as mean±SD. Differences in tumor volume are evaluated using Student's t-test.

References:

[1]. Wedge SR, et al. ZD6474 inhibits vascular endothelial growth factor signaling, angiogenesis, and tumor growth following oral administration. Cancer Res. 2002 Aug 15;62(16):4645-55.
[2]. Hegedus C, et al. Interaction of the EGFR inhibitors gefitinib, vandetanib, pelitinib and neratinib with the ABCG2 multidrug transporter: implications for the emergence and reversal of cancer drug resistance. Biochem Pharmacol. 2012 Aug 1;84(3):260-7.
[3]. Takeda H, et al.


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Vandetanib is effective in EGFR-mutant lung cancer cells with PTEN deficiency. Exp Cell Res. 2013 Feb 15;319(4):417-23.
[4]. Inoue K, et al. Vandetanib, an inhibitor of VEGF receptor-2 and EGF receptor, suppresses tumor development and improves prognosis of liver cancer in mice. Clin Cancer Res. 2012 Jul 15;18(14):3924-33.

## Background

Description: IC50 Value: 40 nM (VEGFR2) [1]; 500 nM (EGFR) [2] Vandetanib is an anti-cancer drug that is used for the treatment of certain tumours of thethyroid gland. It acts as a kinase inhibitor of a number of cell receptors, mainly the vascular endothelial growth factor receptor (VEGFR), the epidermal growth factor receptor (EGFR), and the RET-tyrosine kinase. in vitro: Vandetanib also inhibits VEGFR3 and EGFR with IC50 of 110 nM and 500 nM, respectively. Vandetanib is not sensitive to PDGFRβ, Flt1, Tie-2 and FGFR1 with IC50 of 1.1-3.6 μM, while almost has no activity against MEK, CDK2, c-Kit, erbB2, FAK, PDK1, Akt and IGF-1R with IC50 above 10 μM. Vandetanib inhibits VEGF-, EGF- and bFGF-stimulated HUVEC proliferation with IC50 of 60 nM, 170 nM and 800 nM, with no effect on basal endothelial cell growth. Vandetanib inhibits tumor cell growth with IC50 of 2.7 μM (A549) to 13.5 μM (Calu-6) [2]. Both gefitinib and vandetanib suppressed the activation of EGFR and MAPK in H1650 cells, although phosphorylated AKT levels were not affected. In an H1650 cell xenograft model, vandetanib was also more effective than gefitinib [3]. in vivo: In tumor-bearing mice, vandetanib suppressed phosphorylation of VEGFR-2 and EGFR in tumor tissues, significantly reduced tumor vessel density, enhanced tumor cell apoptosis, suppressed tumor growth, improved survival, reduced number of intrahepatic metastases, and upregulated VEGF, TGF-α, and EGF in tumor tissues [4]. Animals were treated for 28 days with 1 mg/kg/d (DTX1) or 6 mg/kg q4d

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(DTX6) docetaxel with or withoutvandetanib (15 mg/kg/d p.o.) in mice bearing UMSCC2 tumor xenografts. The DTX1 dosing scheme was adjusted to treatment for 10 days followed by 9 days off due to severe gastrointestinal toxicity [5]. Toxicity: Treatment with vandetanib was not associated with serious adverse events, including alanine aminotransferase abnormality, bone marrow suppression, or body weight loss [4]. Clinical trial: N/A


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